

Fig.1.

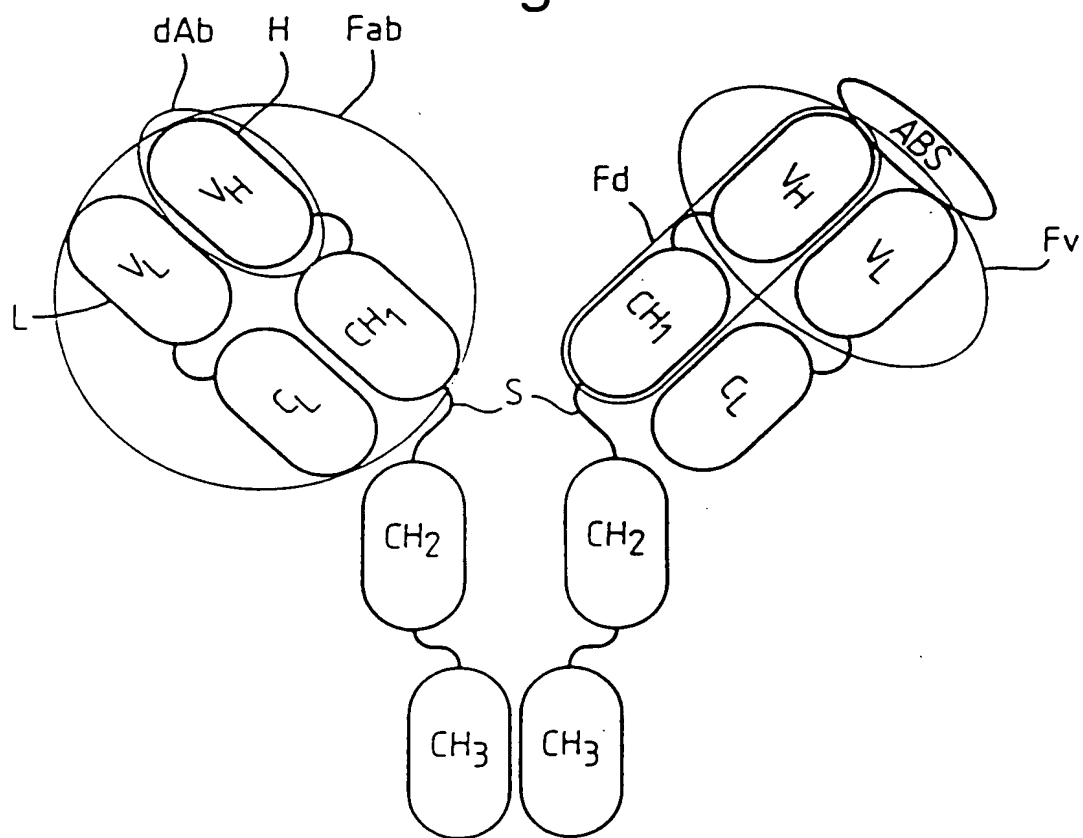




Fig.2 (i).

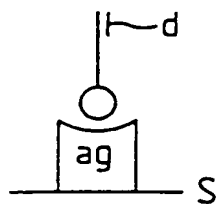
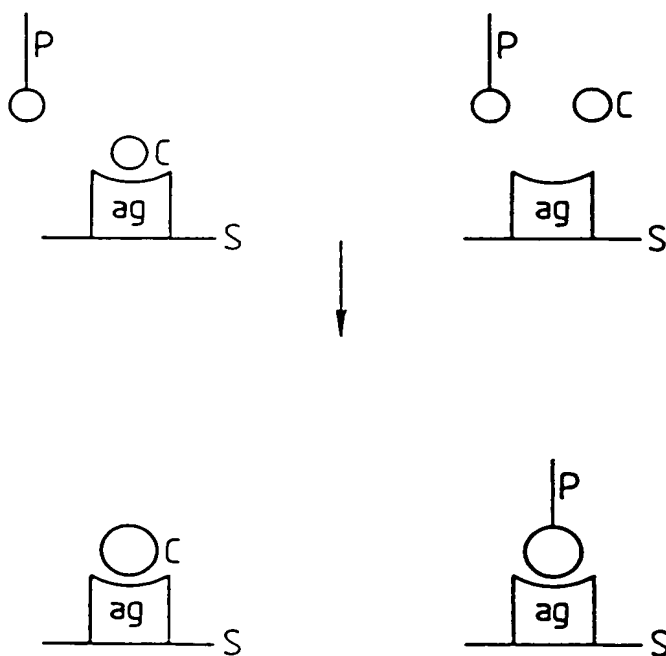


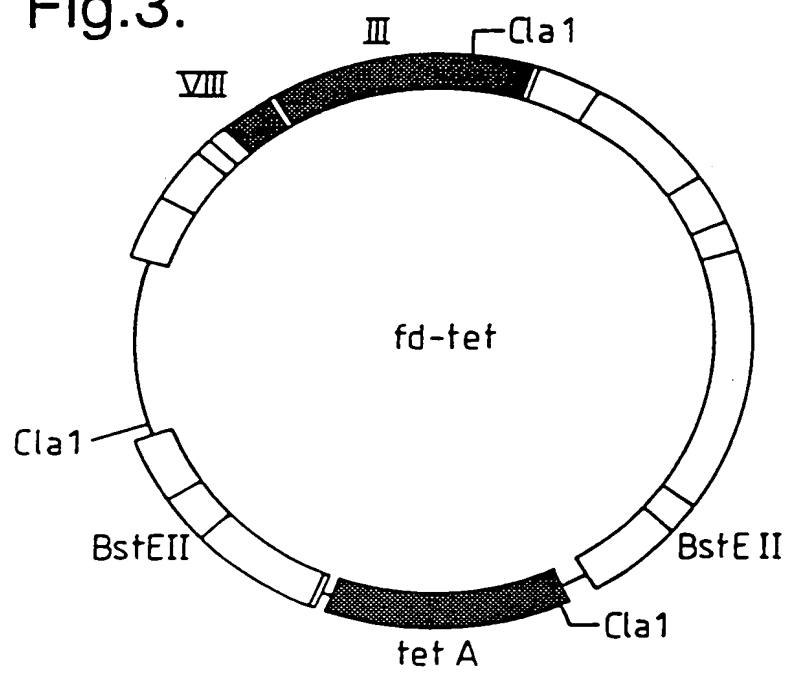
Fig.2 (ii).



09417478, 101399

09417478-101399

Fig.3.



fd - tet
~
cleave with BstEII
~
fill in with Klenow
~
re-ligate
↓
FDT δ Bst
~
in vitro mutagenesis (oligo 1)
↓
FDTPs/Bs
~
in vitro mutagenesis (oligo 2)
↓
FDTPs/Xh

Fig.4 (i).

Oligo 1 (1653) ACA ACT TTC AAC AGT TGA GGA GAC GGT GAC CGT AAG CTT CTG CAG TTG GAC CTG AGC
GGA GTG AGA ATA (1620)
Oligo 2 (1653) ACA ACT TTC AAC AGT TTC CCG TTT GAT CTC GAG CTC CTG CAG TTG GAC CTG
(1704)
Oligo 3 GTC GTC TTT CCA GAC GTT AGT

Fig.4 (ii).

GENE III
SIGNAL
CLEAVAGE SITE
(1624)
A TCT CAC TCC GCT
Q V Q L Q V T V S S
B TCT CAC TCC GCT CAG GTC CAA CTG CAG AAG CTT ACG GTC ACC GTC TCC TCA ACT GTT GAA AGT
PstI BstEII
Q V Q L Q L E I K R
C TCT CAC TCC GCT CAG GTC CAA CTG CAG GAG CTC GAG ATC AAACGG GAA ACT GTT GAA AGT
PstI XhoI
GENE III

Fig.5.

rbs M K Y L L P T A A
 GCATGCAAATTCTATTTCAAGGAGACAGTCATAATGAAATACCTATTGCCTACGGCAGCC
 10 20 30 40 50 60
 SphI
 PelB leader
 A G L L L L A A O P A M A Q V Q L Q E S
 GCTGGATTGTTATTACTCGCTGCCCAACCAGCGATGGCCCAGGTGCAGCTGCAGGAGTCA
 70 80 90 100 110 120
 PstI
 G P G L V A P S Q S L S I T C T V S G F
 GGACCTGGCCTGGTGGCGCCCTCACAGAGCCTGTCCATCACATGCACCGTCTCAGGGTTC
 130 140 150 160 170 180
 S L T G Y G V N W V R Q P P G K G L E W
 TCATTAACCGGCTATGGTGTAAACTGGGTTCGCCAGCCTCCAGGAAAGGGTCTGGAGTGG
 190 200 210 220 230 240
 VHD1.3
 L G M I W G D G N T D Y N S A L K S R L
 CTGGGAATGATTTGGGGTGATGGAAACACAGACTATAATTCAGCTCTCAAATCCAGACTG
 250 260 270 280 290 300
 S I S K D N S K S Q V F L K M N S L H T
 AGCATCAGCAAGGACAACCTCCAAGAGCCAAGTTTCTTAAAAATGAACAGTCTGCACACT
 310 320 330 340 350 360
 D D T A R Y Y C A R E R D Y R L D Y W G
 GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
 370 380 390 400 410 420
 Linker Peptide
 Q G T T V T V S S G G G G S G G G G S G
 CAAGGCACCAAGGTACCGTCTCCTCAgggtggaggcggttcaggcgagggtggctctggc
 430 440 450 460 470 480
 BstEII
 G G G S D I E L T Q S P A S L S A S V G
 ggtggcggtatcgGACATCGAGCTCACTCAGTCTCCAGCCTCCCTTTCTGCGTCTGTGGGA
 490 500 510 520 530 540
 SacI

09417478-101399

Fig.5 (Cont).

E T V T I T C R A S G N I H N Y L A W Y
GAAACTGTCACCATCACATGTCGAGCAAGTGGGAATATTCACAATTATTTAGCATGGTAT
550 560 570 580 590 600

Q Q K Q G K S P Q L L V Y Y T T T L A D
CAGCAGAAACAGGGAAAATCTCCTCAGCTCCTGGTCTATTATACAACAACCTTAGCAGAT
610 620 630 640 650 660

VKD1.3

G V P S R F S G S G S G T Q Y S L K I N
GGTGTGCCATCAAGGTTTCAGTGGCAGTGGATCAGGAACACAATATTCTCTCAAGATCAAC
670 680 690 700 710 720

S L Q P E D F G S Y Y C Q H F W S T P R
AGCCTGCAACCTGAAGATTTTGGGAGTTATTACTGTCAACATTTTGGAGTACTCCTCGG
730 740 750 760 770 780

Myc Tag (TAG1)

T F G G G T K L E I K R E O K L I S E E
ACGTTTCGGTGGAGGGACCAAGCTCGAGATCAAACGGGAACAAAACTCATCTCAGAAGAG
790 800 810 820 830 840

XhoI

D L N * *

GATCTGAATTAATAATGATCAAACGGTAATAAGGATCCAGCTCGAATTC
850 860 870 880

EcoRI

Fig.6.

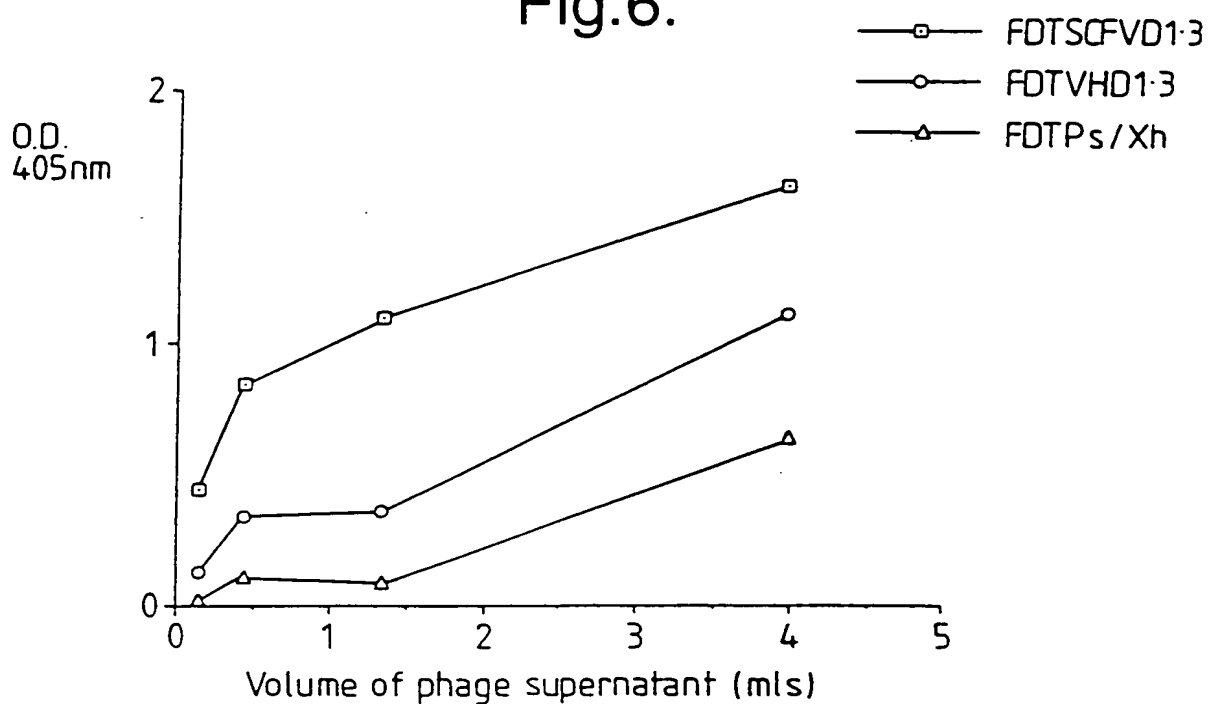
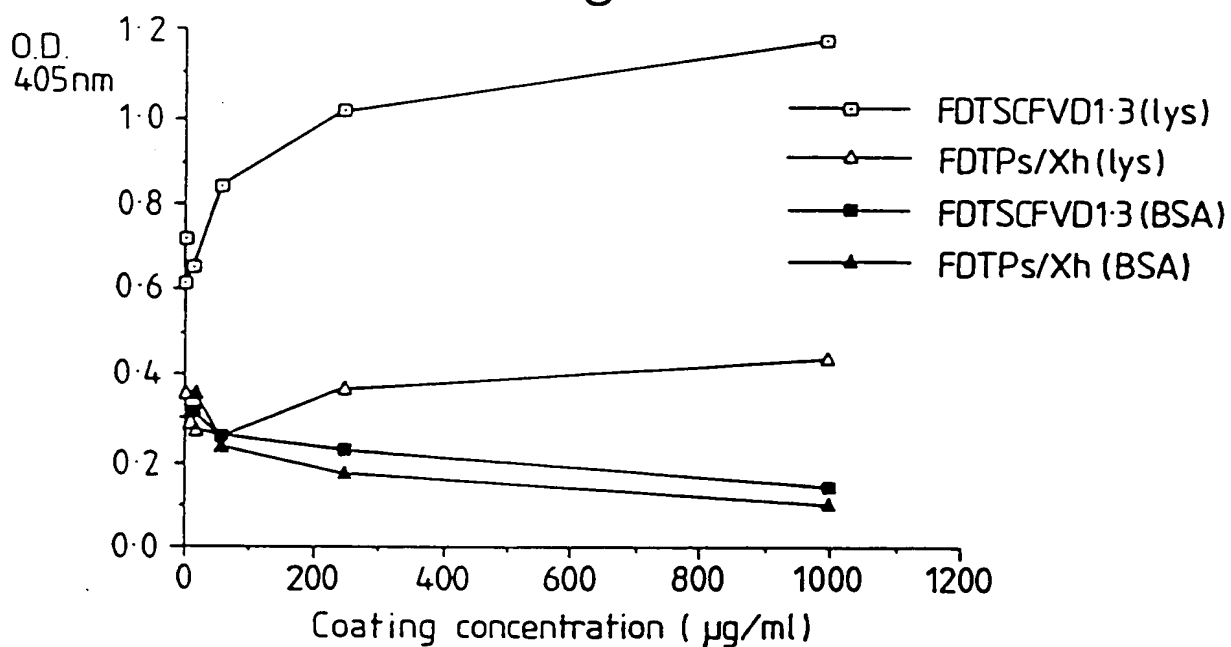
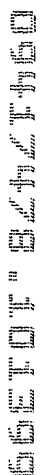


Fig.7.



05148-1019



05148-1019

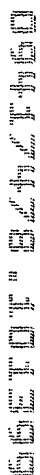


Fig.10.

M K Y L L P T A A
GCATGCAAATTCTATTTCAAGGAGACAGTCATAATGAAATACCTATTGCCTACGGCAGCC
10 20 30 40 50 60

A G L L L L A A Q P A M A Q V Q L Q E S
GCTGGATTGTTATTACTGCTGCCCAACCAGCGATGGCCCAGGTGCGCTGCAGGAGTCA
70 80 90 100 110 120

G P G L V A P S Q S L S I T C T V S G F
GGACCTGGCCTGGTGGCGCCCTCACAGAGCCTGTCCATCACATGCACCGTCTCAGGGTTC
130 140 150 160 170 180

S L T G Y G V N W V R Q P P G K G L E W
TCATTAAACCGGCTATGGTGTAAACTGGGTTCGCCAGCCTCCAGGAAAGGGTCTCGAGTGG
190 200 210 220 230 240

L G M I W G D G N T D Y N S A L K S R L
CTGGGAATGATTTGGGGTGATGGAAACACAGACTATAATTACAGCTCTCAAATCCAGACTG
250 260 270 280 290 300

S I S K D N S K S Q V F L K M N S L H T
AGCATCAGCAAGGACAACCTCCAAGAGCCAAGTTTTCTTAAAAATGAACAGTCTGCACACT
310 320 330 340 350 360

D D T A R Y Y C A R E R D Y R L D Y W G
GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
370 380 390 400 410 420

Q G T T V T V S S A S T K G P S V F P L
CAAGGCACCAAGGTACCGTCTCCTCAGCCTCCACCAAGGGCCCATGGTCTTCCCCCTG
430 440 450 460 470 480

A P S S K S T S G G T A A L G C L V K D
GCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGCCCTGGGCTGCCTGGTCAAGGAC
490 500 510 520 530 540

Fig.10 (Cont 1).

Y F P E P V T V S W N S G A L T S G V H
TACTTCCCCGAACCGGTGACGGTGTCTGTGGAACTCAGGCGCCCTGACCCAGCGGGGTGCAC
550 560 570 580 590 600

T F P A V L Q S S G L Y S L S S V V T V
ACCTTCCCGGCTGTCTACAGTCTCTAGGACTCTACTCCCTCAGCAGGGTGGTGACCGTG
610 620 630 640 650 660

P S S S L G T Q T Y I C N V N H K P S N
CCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAAC
670 680 690 700 710 720

T K V D K K V E P K S S * *
ACCAAGGTGACAAGAAAGTTGAGCCCAATCTTCATAATAACCCGGGAGCTTGCATGCA
730 740 750 760 770 780

M K Y L L P T A A A G L
AATTCTATTTCAGGAGACAGTCATAATGAAATACCTATTGCTACGGCAGCCGCTGGAT
790 800 810 820 830 840

L L L A A Q P A M A D I E L T Q S P A S
TGTTATTACTGCTGCCCCAACCCAGCGATGGCCGACATCGAGCTCACCCAGTCTCCAGCCT
850 860 870 880 890 900

L S A S V G E T V T I T C R A S G N I H
CCCTTCTGCGTCTGTGGGAGAACTGTACCATCACATGTGAGCAAGTGGGAATATT
910 920 930 940 950 960

N Y L A W Y Q Q K Q G K S P Q L L V Y Y
ACAATTATTTAGCATGGTATCAGCAGAAACAGGGAAAATCTCTCTCAGCTCCTGGTCTATT
970 980 990 1000 1010 1020

Fig.10 (Cont 2).

T T T L A D G V P S R F S G S G S G T Q
ATACAACAACCTTAGCAGATGGTGTGCCATCAAGGTTGAGTGGCAGTGGATCAGGAACAC
1030 1040 1050 1060 1070 1080

Y S L K I N S L Q P E D F G S Y Y C Q H
AATATTCTCTCAAGATCAACAGCCTGCAGCCTGAAGATTTTGGGAGTTATTACTGTCAAC
1090 1100 1110 1120 1130 1140

F W S T P R T F G G G T K L E I K R T V
ATTTTGGGAGTACTCTCTGGACGTTCTGGTGGAGGCCAAGCTCGAGATCAAACGGACTG
1150 1160 1170 1180 1190 1200

A A P S V F I F P P S D E Q L K S G T A
TGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAAGT
1210 1220 1230 1240 1250 1260

S V V C L L N N F Y P R E A K V Q W K V
CCTCTGTTGTGTGCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGGAAGG
1270 1280 1290 1300 1310 1320

D N A L Q S G N S Q E S V T E Q D S K D
TGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCAACAGAGCAGGACAGCAAGG
1330 1340 1350 1360 1370 1380

S T Y S L S S T L T L S K A D Y E K H K
ACAGCACCTACAGCCTCAGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGAGAAACACA
1390 1400 1410 1420 1430 1440

V Y A C E V T H Q G L S S P V T K S F N
AAGTCTACGCCCTGCGAAGTCAACCATCAGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCA
1450 1460 1470 1480 1490 1500

R G E S * *
ACCGCGGAGAGTCATAGTAAGAATTC
1510 1520

09447478 101399
55EET 8272760

Fig.10 (Cont 3).

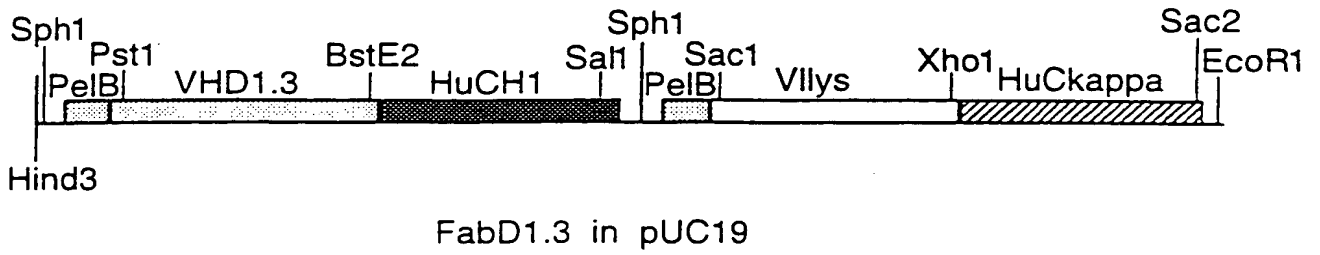


Fig.11.

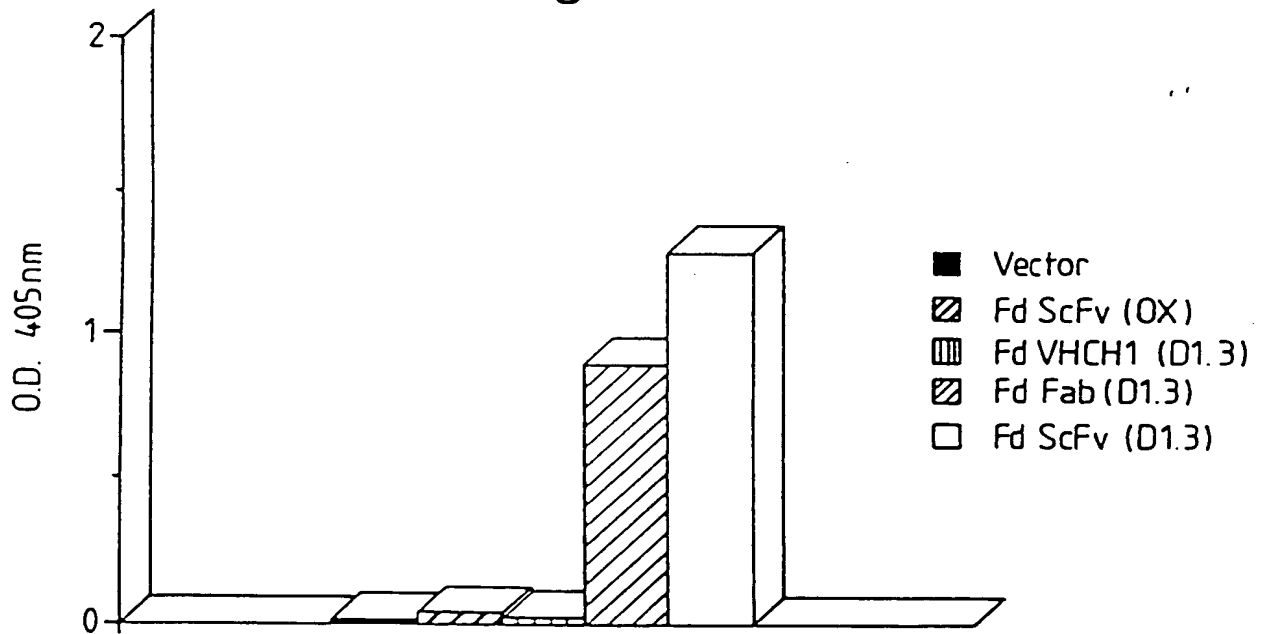


Fig.12a.

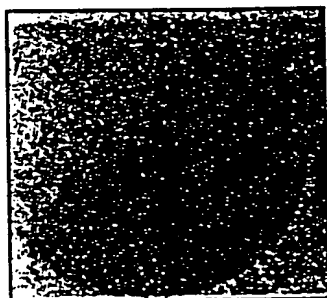


Fig.12b.

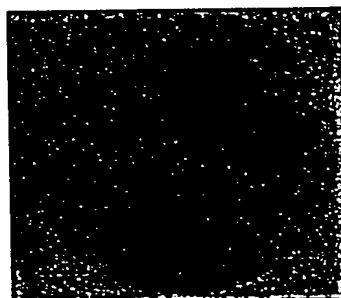


Fig.13.

Q V Q L Q E S G G G L V Q P G G
CAG GTG CAG CTG CAG GAG TCA GGA GGA GGC TTG GTA CAG CCT GGG GGT
PstI
S L R L S C A T S G F T F S N Y
TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC AGT AAT TAC
Y M G W V R Q P P G K A L E W L
TAC ATG GGC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG
G S V R N K V N G Y T T E Y S A
GGT TCT GTT AGA AAC AAA GTT AAT GGT TAC ACA ACA GAG TAC AGT GCA
S V K G R F T I S R D N F Q S I
TCT GTG AAG GGG CGG TTC ACC ATC TCC AGA GAT AAT TTC CAA AGC ATC
L Y L Q I N T L R T E D S A T Y
CTC TAT CTT CAA ATA AAC ACC CTG AGA ACT GAG GAC AGT GCC ACT TAT
Y C A R G Y D Y G A W F A Y W G
TAC TGT GCA AGA GGC TAT GAT TAC GGG GCC TGG TTT GCT TAC TGG GGC
Q G T L V T v s s g g g g s g g g g s
CAA GGG ACC CTG GTC ACC gtc tcc tca ggaggaggcggttcaggcggagggtggctct
BstEII
g g g g s d i E L T Q T P L S L P V
ggcgggtggcggtcgac atc GAG CTC ACC CAA ACT CCA CTC TCC CTG CCT GTC
SacI
S L G D Q A S I S C R S S Q S I
AGT CTT GGA GAT CAA GCC TCC ATC TCT TGC AGA TCT AGT CAG AGC ATT
V H S N G N T Y L E W Y L Q K P
GTA CAT AGT AAT GGA AAC ACC TAT TTA GAA TGG TAC CTG CAG AAA CCA
PstI
G Q S P K L L I Y K V S N R F S
GGC CAG TCT CCA AAG CTC CTG ATC TAC AAA GTT TCC AAC CGA TTT TCT
G V P D R F S G S G S G T D F T
GGG GTC CCA GAC AGG TTC AGT GGC AGT GGA TCG GGG ACA GAT TTC ACA
L K I S R V E A E D L G V Y Y C
CTC AAG ATC AGC AGA GTG GAG GCT GAG GAT CTG GGA GTT TAT TAC TGC
F Q G S H V P Y T F G G G T K L
TTT CAA GGT TCA CAT GTT CCG TAC ACG TTC GGA GGG GGG ACC AAG CTC
E I K R
GAG ATC AAA CGG
XhoI

SECRET 844743-10199

Fig.14.

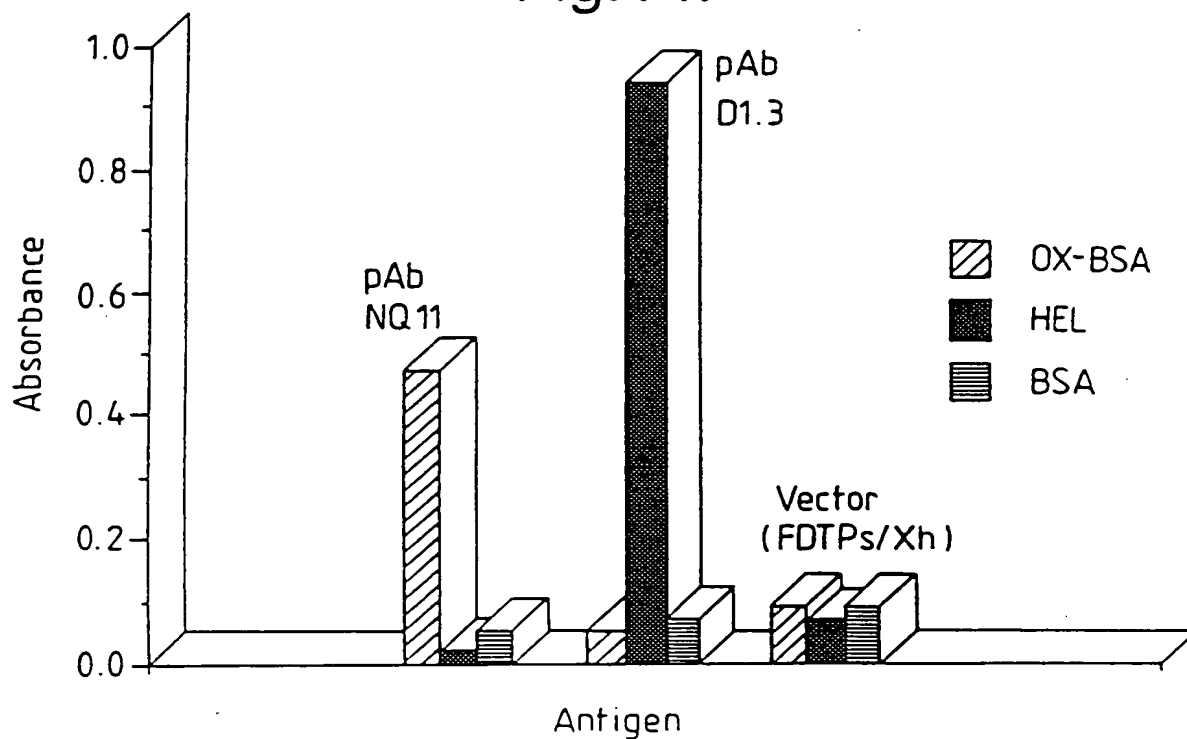


Fig.15.

5' END

TCT CAC AGT GCA CAA ACT GTT GAA CGG ACA CCA GAA ATG CCT GTT CTG
 ApaL1

3' END

K A A L G L K
 AAA GCC GCT CTG GGG CTG AAA GCG GCC GCA GAA ACT GTT GAA AGT etc.
 Not I

Fig.16 (i).

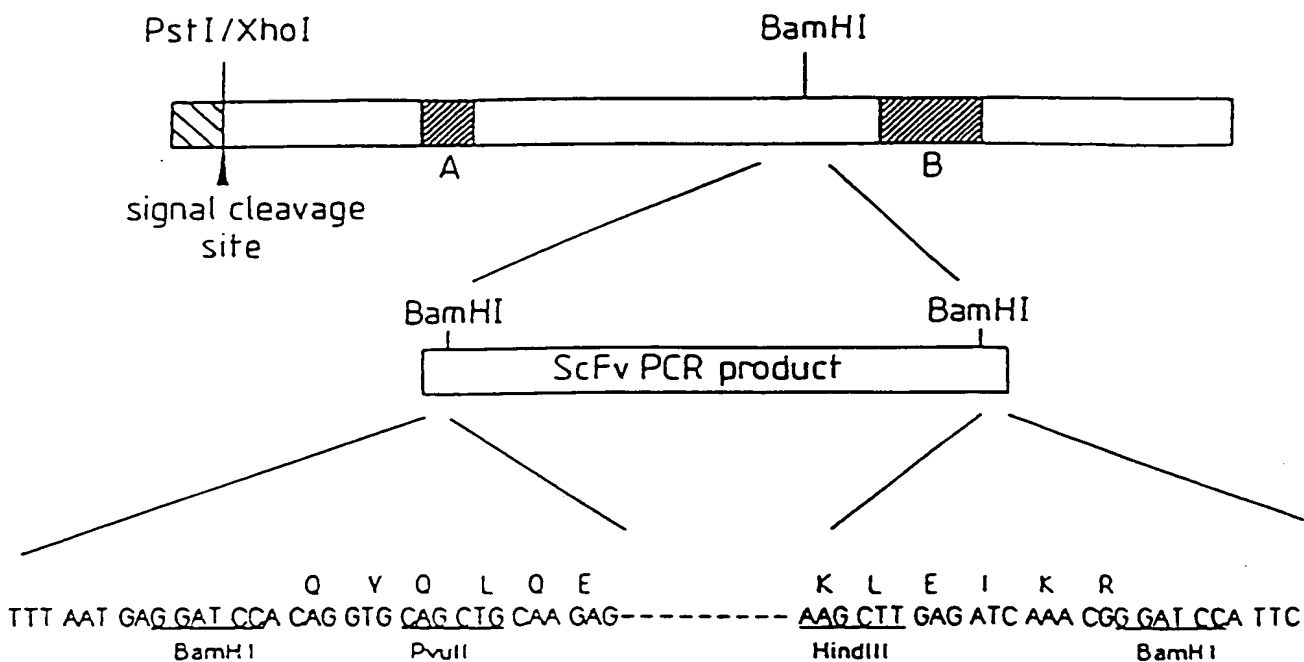


Fig.16 (ii).

A (1834) 5' GAG GGT GGT GGC TCT
 " " "C " "
 " " "C " "
 " " "C " ACT 3' (1839)

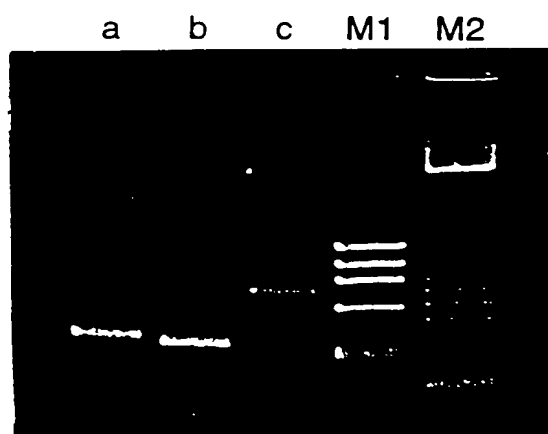
B (2284) 5' - GGC GGC GGC TCT
 - GGT GGT GGT -
 - " GGC GGC -
 GAG - " GGC -
 " - " GGT -
 - " - GGC -
 - " - GGT -
 - " " GGC - 3' (2379)

Reverse complement of mutagenic
 oligo G3Bamlink

5' GAG GGT GGC GGA TCC
 T
 GAG GGT GGC GG 3'

0941743-101399

Fig.18.



66EFOF"8242T460

Fig.19.

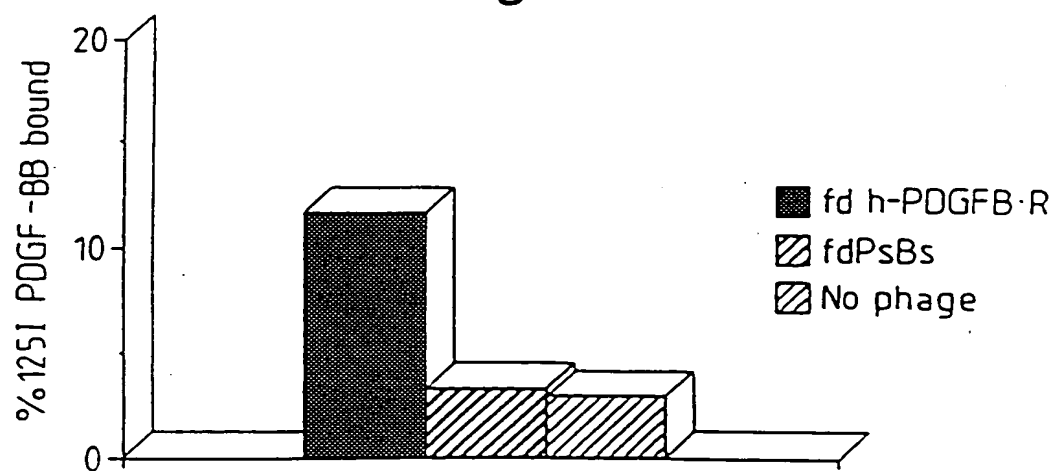


Fig.20.

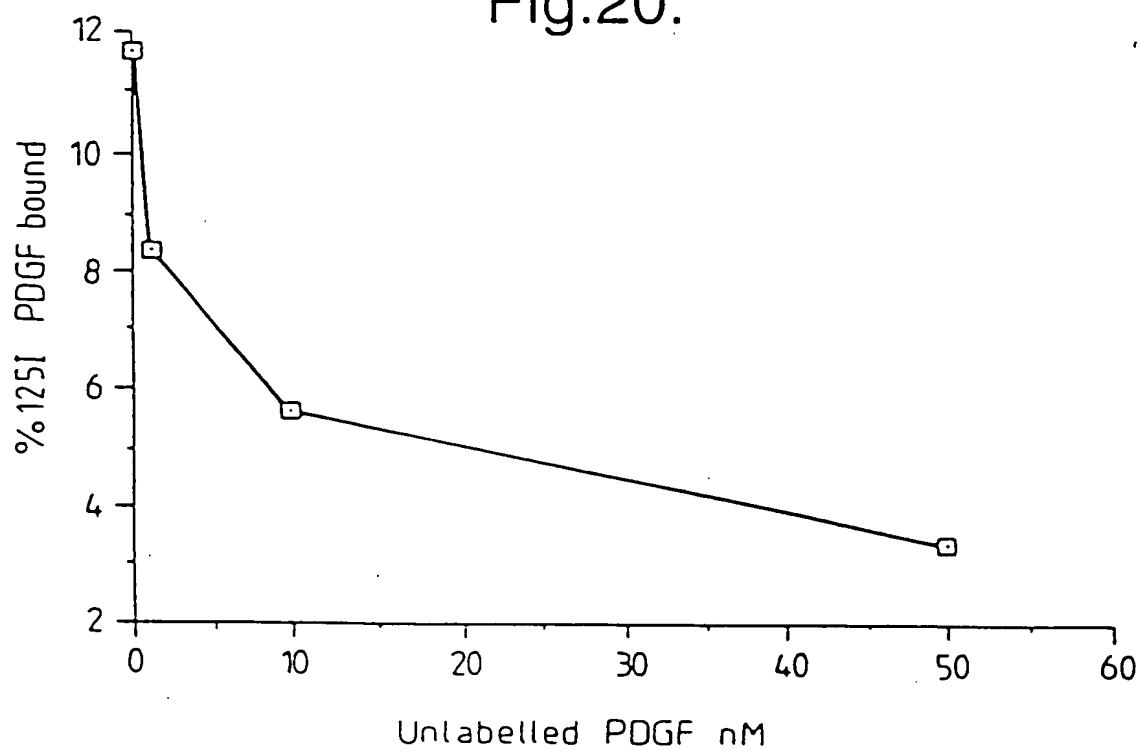


Fig.21.

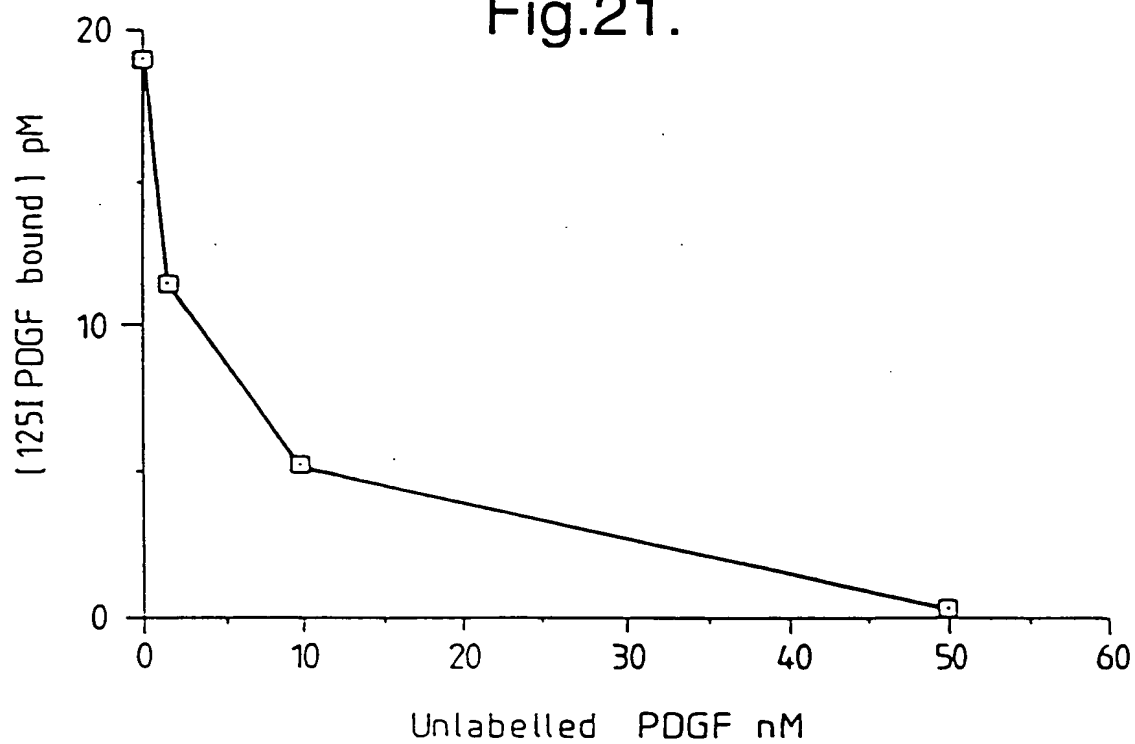


Fig.22.

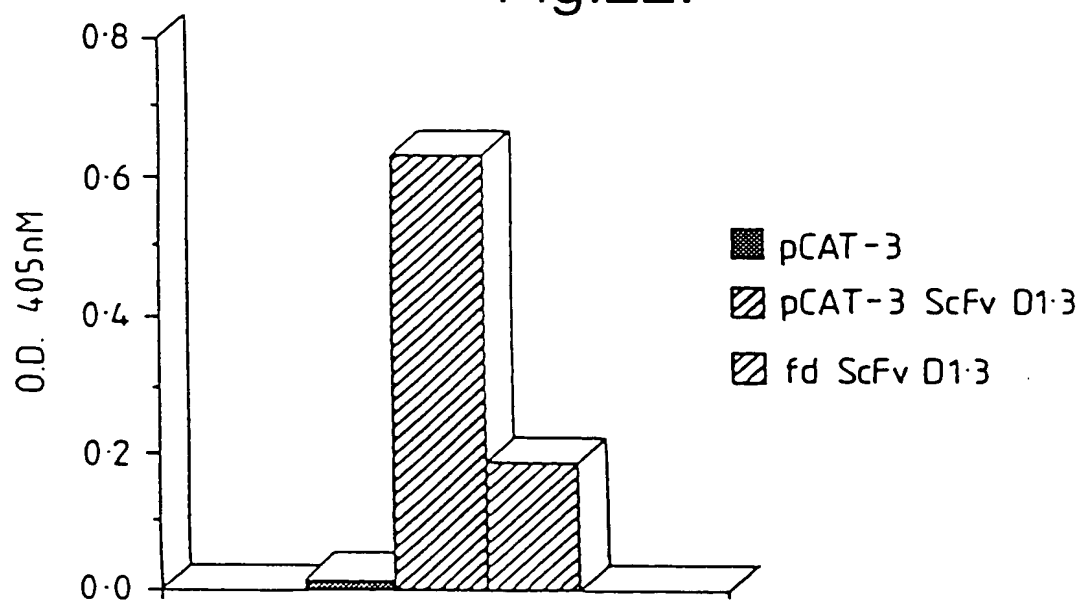


Fig.23(i)

d
M

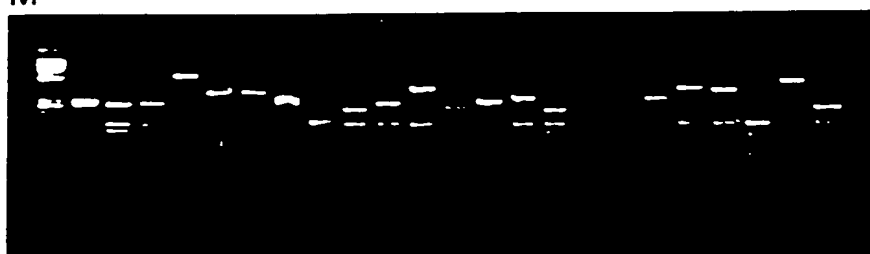


Fig.23(ii)

M

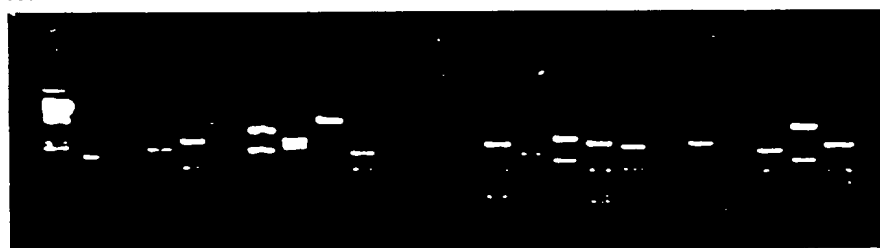


Fig.24.

VH sequences

from combinatorial library:

	CDR1	CDR2	CDR3	
A	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x4 1
B	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x9 1
C	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x3 1
D	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x3 1
E	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x2 1
F	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x1 1
G	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x1 1
H	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x1 1

from hierarchical library VH-rep x Vκ-d:

I	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1
J	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1
K	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x3 1
L	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x3 1
M	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1
N	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1
O	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1
P	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1
Q	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1
R	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1
S	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x3 1
T	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS x6 1
U	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1
V	QVQLQSGGELARPGASVTHSKASGYTFT	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVYYCAR	HQGGTTTVSS 1

Fig.24 (Cont).

Vx sequences

from combinatorial library:

	CDR1	CDR2	CDR3		
a	DIELTQSPSSLSASLGERVSLTC	WLQKPGDGIKRLIY	LOVASYPYPT	FGAGTKLEIKRA	x3
b	DIELTQSPAIMSASPGKVTNTC	WYQKSGASPKVMIIY	QYSGYPLT	FGAGTKLEIKRA	x3
c	DIELTQSPPTTHAASPGKVTITC	WYQKPGFSPKLLIY	QYSGYPLT	FGAGTKLEIKRA	x2
d	DIELTQSPPTTHAASPGKVTITC	WYQKPGFSPKLLIS	QYSGYPLT	FGAGTKLEIKRA	x9
e	DIELTQSPAIMSASPGKVTITC	WYQKPGCTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	x4
f	DIELTQSPAIMSASPGKVTITC	WYQKSGTSPKRMIIY	QYSGYPLT	FGAGTKLEIKRA	VI
g	DIELTQSPAIMSASPGKVTNTC	WYQKPGASPKRMIIY	QYSGYPLT	FGAGTKLEIKRA	VI

from hierarchical library VH-B x Vx-rep:

	CDR1	CDR2	CDR3		
h	DIELTQSPAIMSASPGKVTNTC	WYQKSGTSPKRMIIY	QYSGYPLT	FGAGTKLEIKRA	x4
i	DIELTQSPAIMSASPGKVTITC	WYQKPGTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	VI
j	DIELTQSPPTTHAASPGKVTITC	WYQKPGFSPKLLIY	QYSGYPLT	FGAGTKLEIKRA	VI
k	DIELTQSPPTTHAASPGKVTITC	WYQKPGFSPKLLIY	QYSGYPLT	FGAGTKLEIKRA	VI
l	DIELTQSPPTTHAASPGKVTITC	WYQKPGFSPKLLIY	QYSGYPLT	FGAGTKLEIKRA	VI
m	DIELTQSPPTTHAASPGKVTITC	WYQKPGFSPKLLIY	QYSGYPLT	FGAGTKLEIKRA	VI
n	DIELTQSPPTTHAASPGKVTITC	WYQKPGFSPKLLIY	QYSGYPLT	FGAGTKLEIKRA	VI
o	DIELTQSPPTTHAASPGKVTITC	WYQKPGFSPKLLIY	QYSGYPLT	FGAGTKLEIKRA	VI
p	DIELTQSPPTTHAASPGKVTITC	WYQKPGTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	VI
q	DIELTQSPPTTHAASPGKVTITC	WYQKPGTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	VI
r	DIELTQSPPTTHAASPGKVTITC	WYQKPGTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	VI
s	DIELTQSPPTTHAASPGKVTITC	WYQKPGTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	VI
t	DIELTQSPPTTHAASPGKVTITC	WYQKPGTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	VI
u	DIELTQSPPTTHAASPGKVTITC	WYQKPGTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	VI
v	DIELTQSPPTTHAASPGKVTITC	WYQKPGTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	VI
w	DIELTQSPPTTHAASPGKVTITC	WYQKPGTSPKLMIIY	QYSGYPLT	FGAGTKLEIKRA	VI

Fig.25.

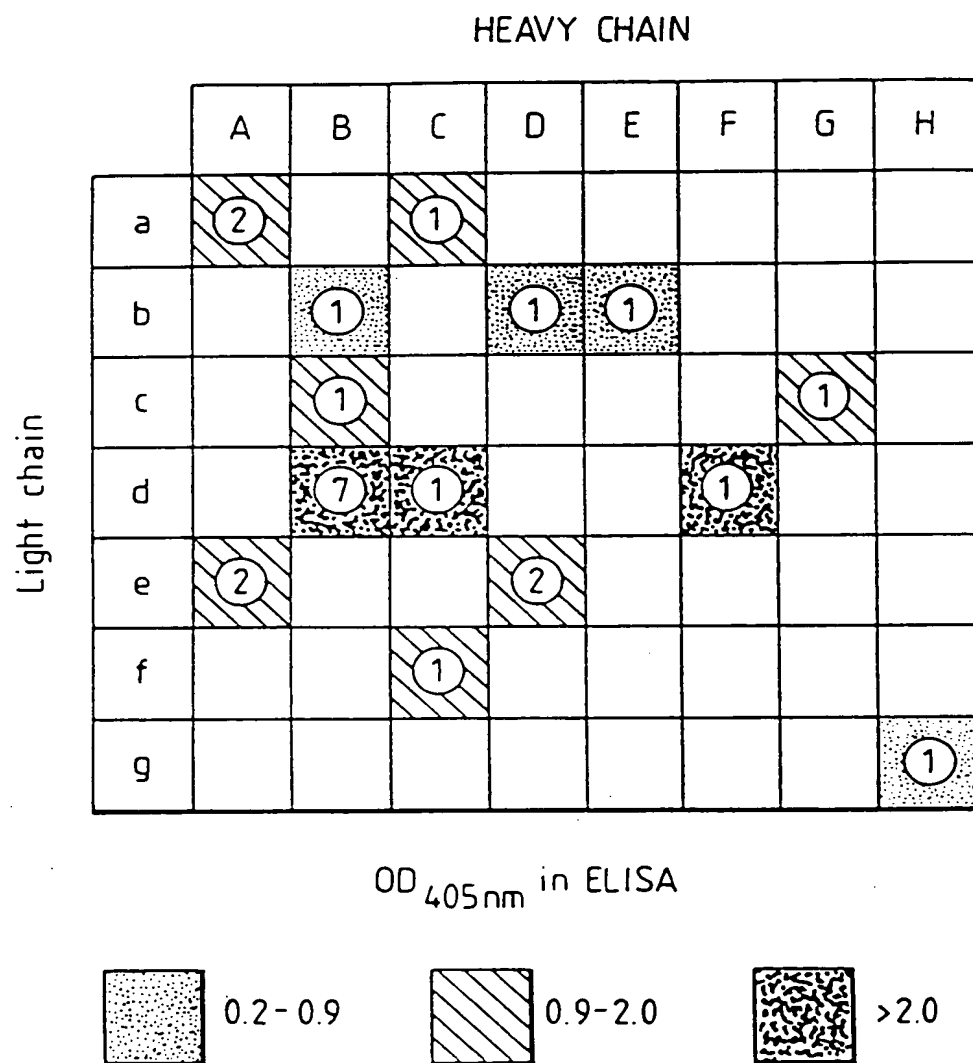


Fig.26(a).

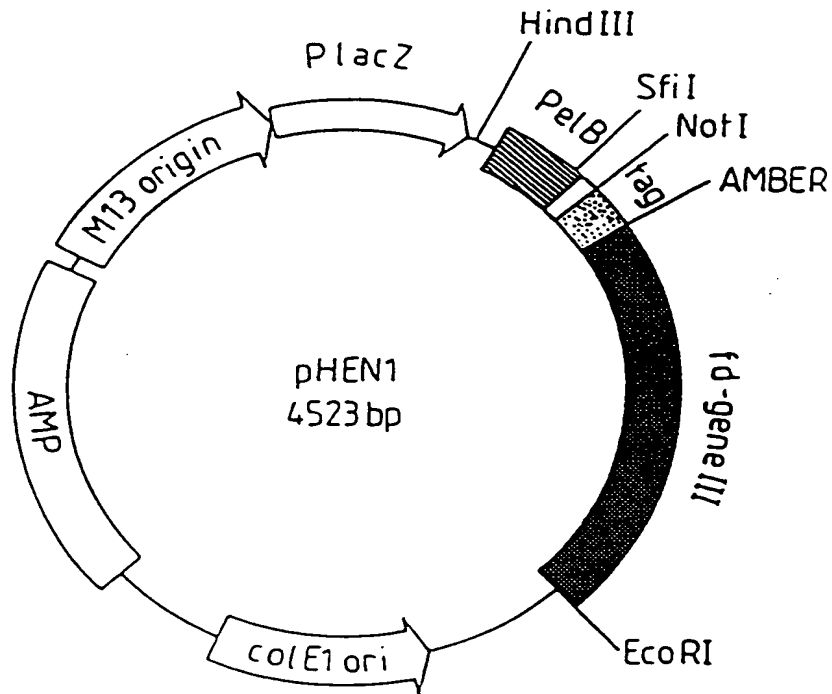


Fig.26(b).

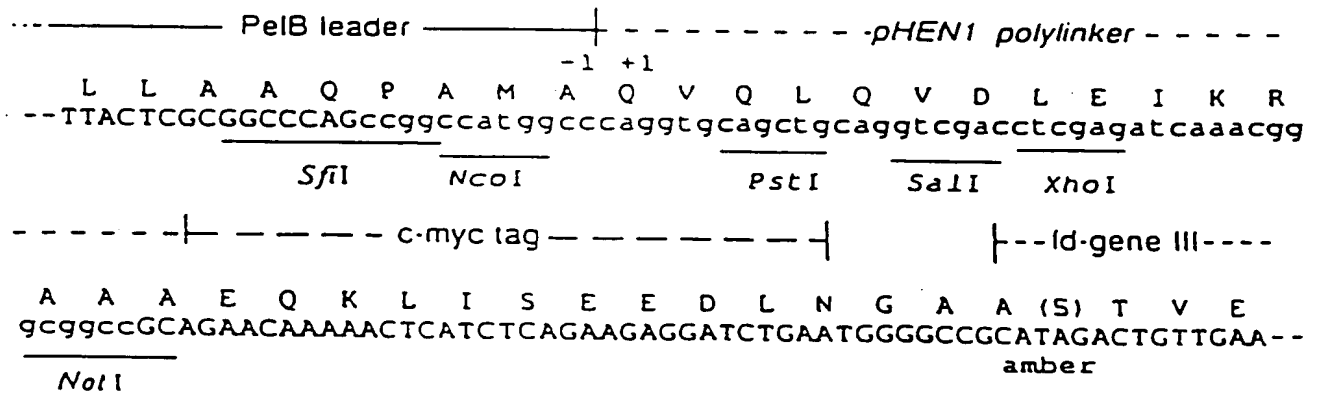
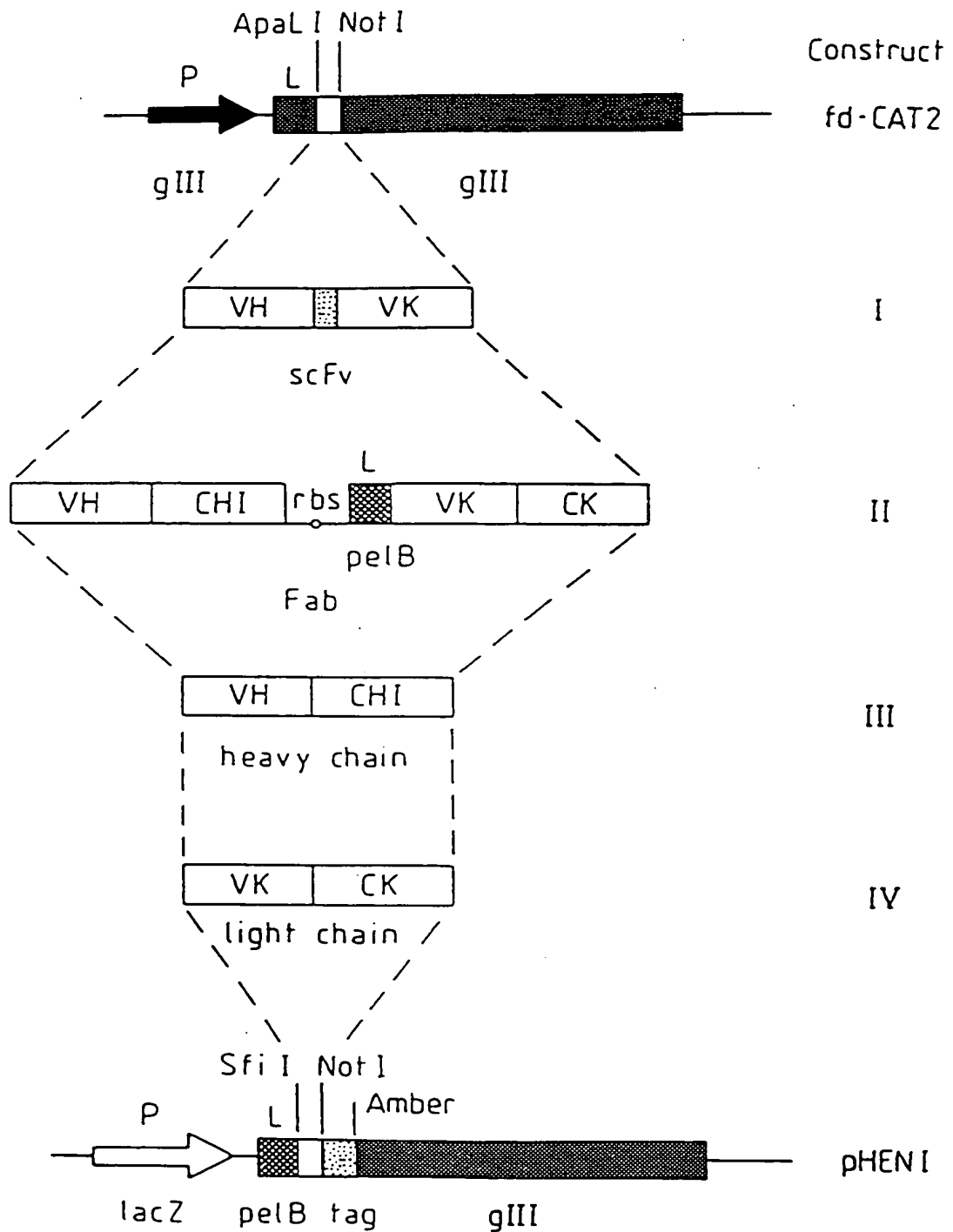


Fig.27.



66EFOF"824ZT460

Fig.28.

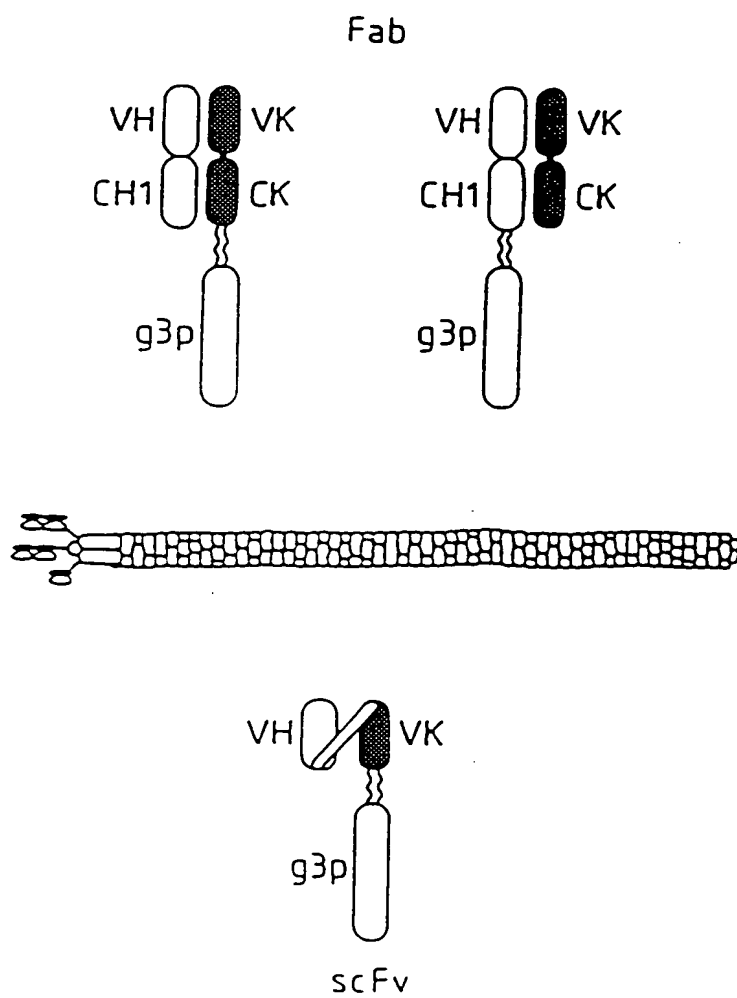


Fig.29.

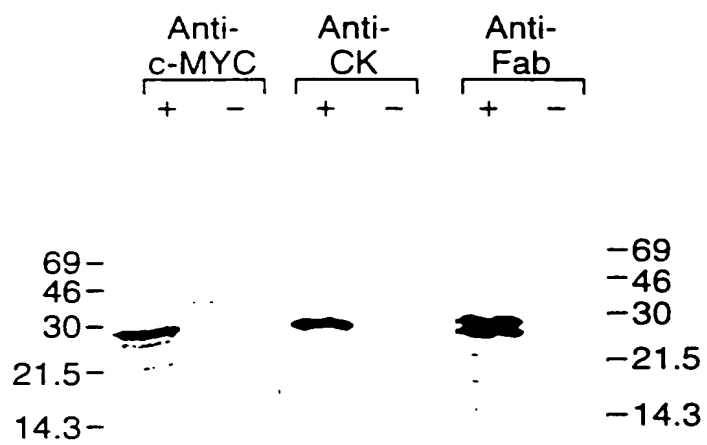


Fig.30.

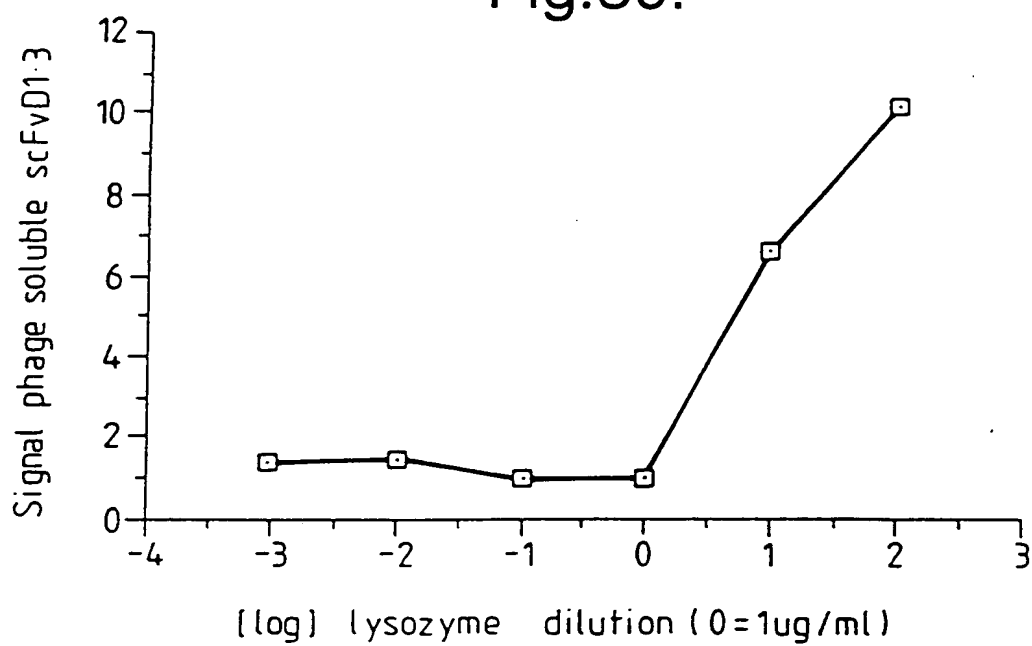


Fig.31.

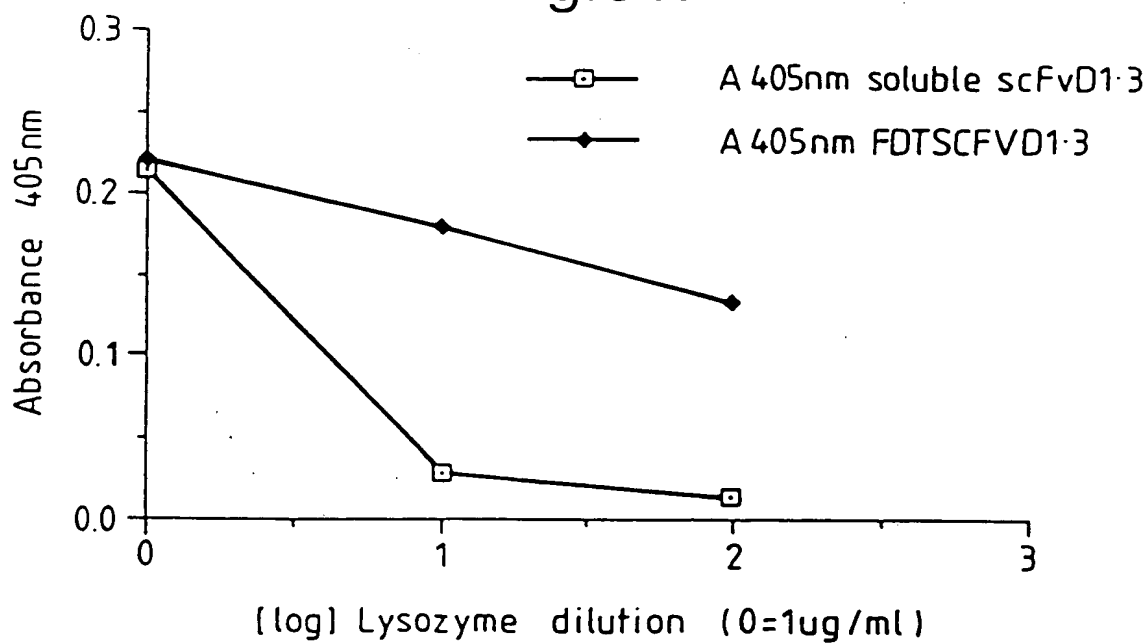


Fig.32.

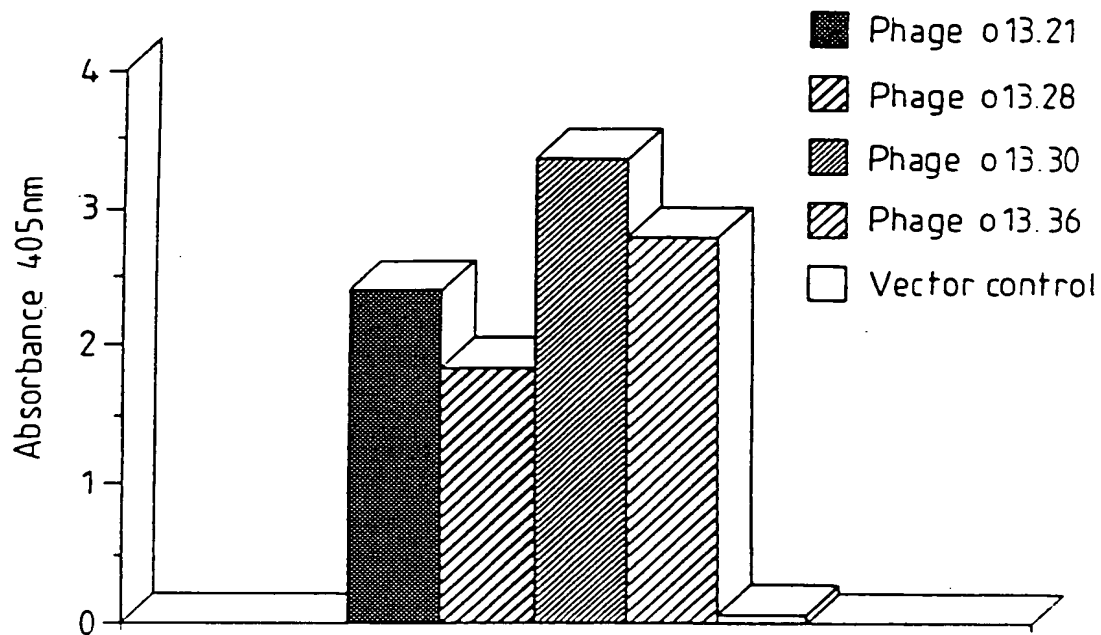


Fig.33.

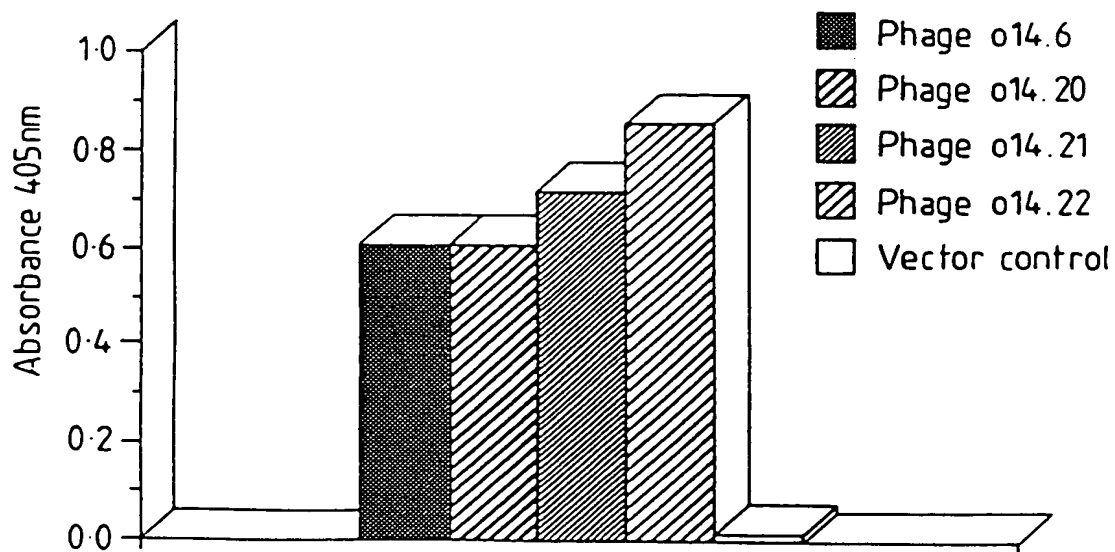


Fig.34.

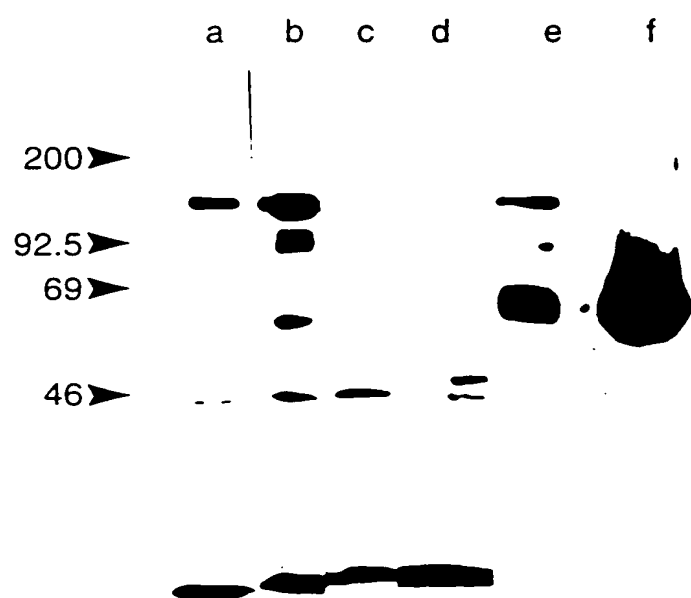


Fig.35A.

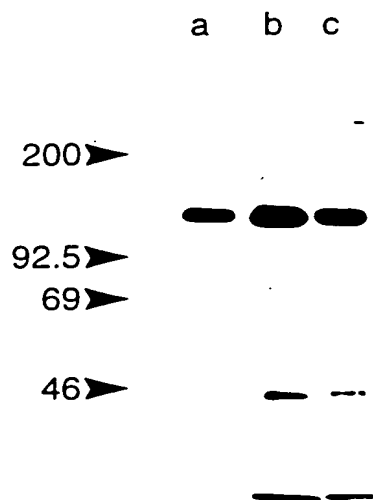


Fig.35B.

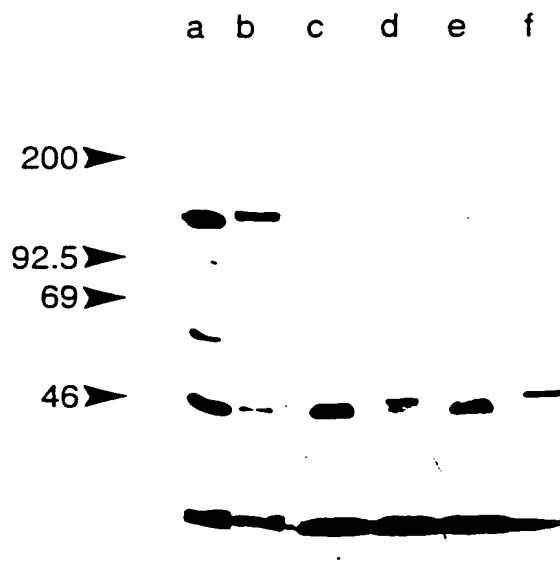


Fig.36.

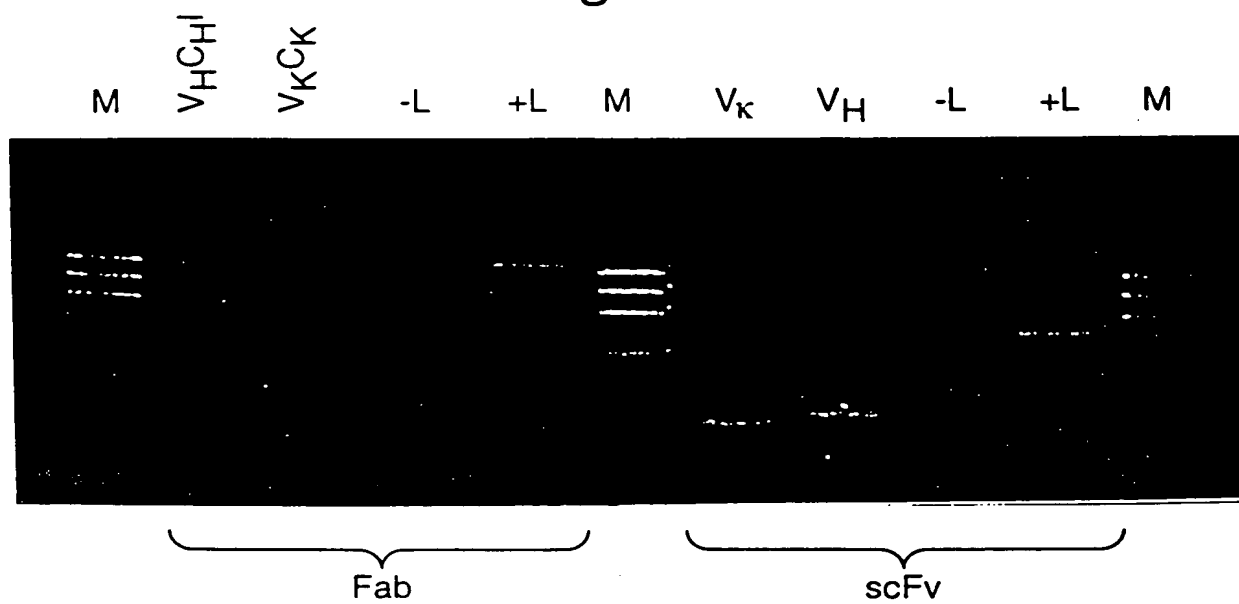


Fig.37.

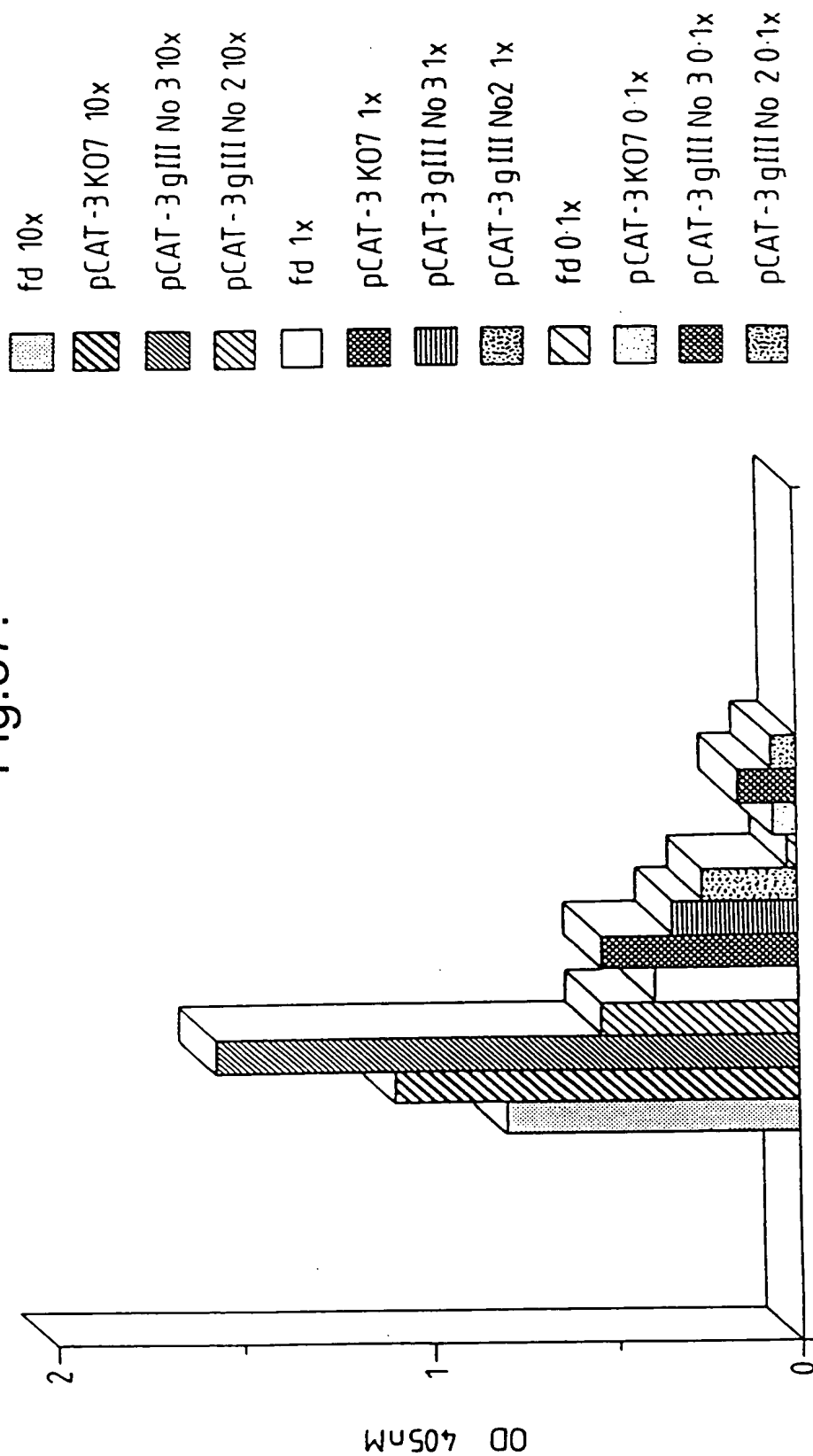


Fig.38A.

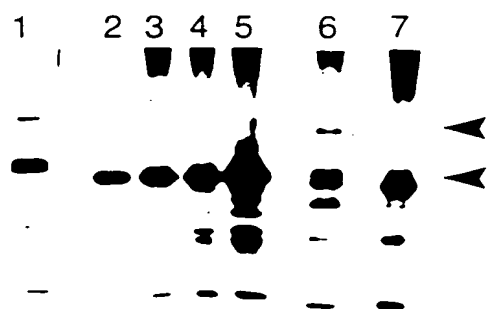


Fig.38B.

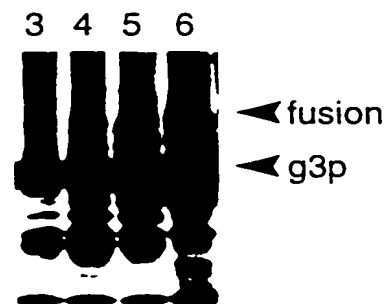


Fig.39.

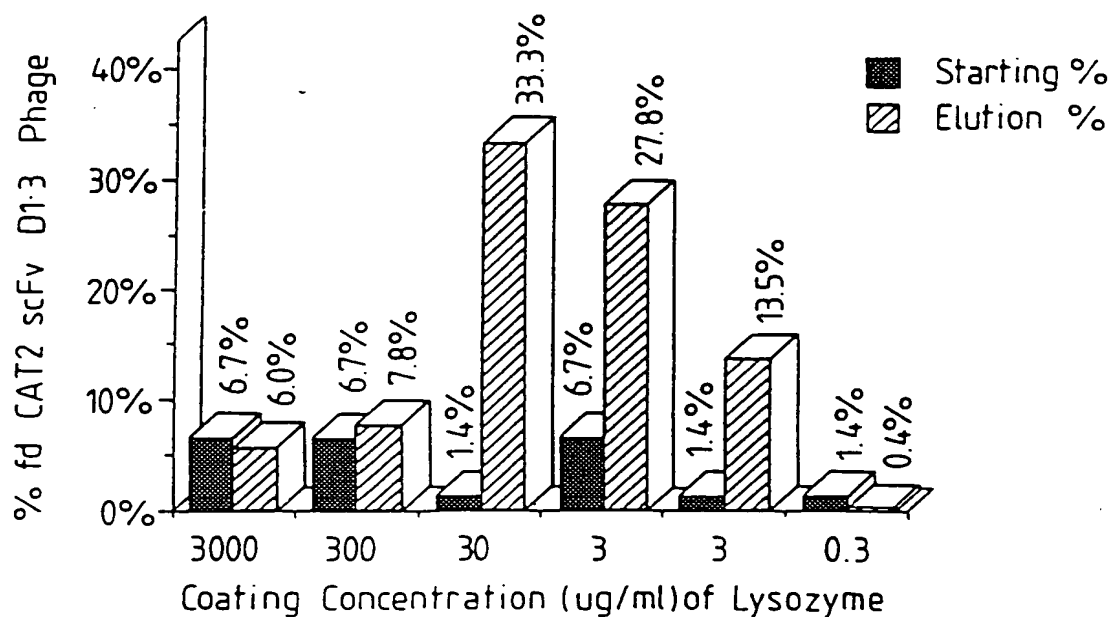


Fig.40.

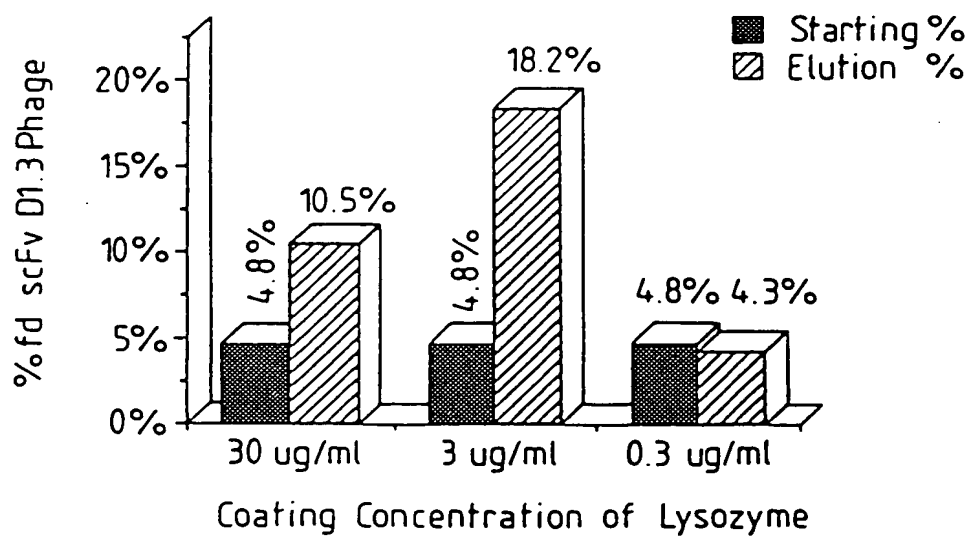


Fig.41.

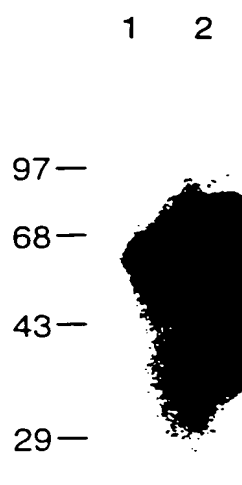


Fig.42.

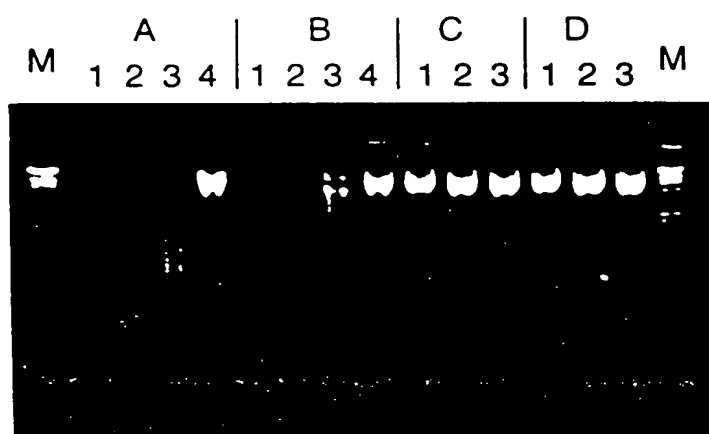


Fig.43.

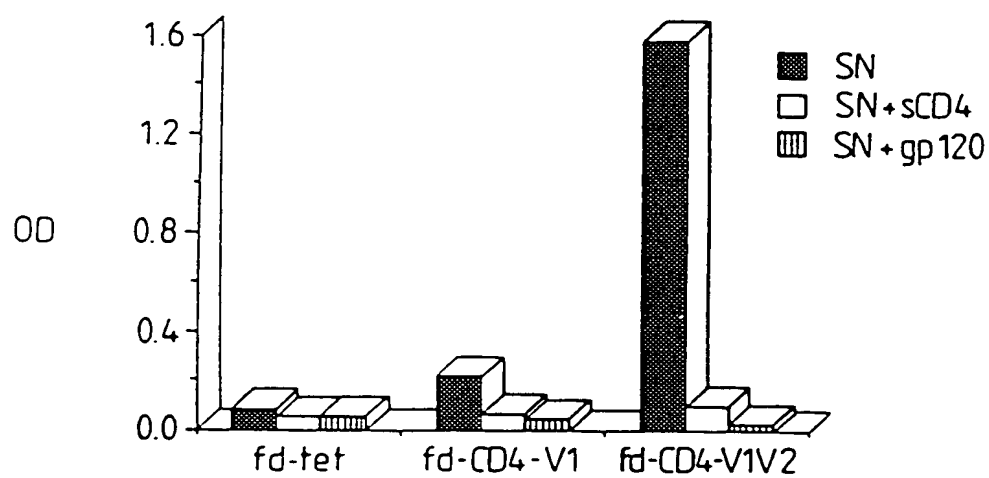


Fig.44 (i).

10	20	30	40	50	60	70	80	90
TTCTATTCTCACAGTGCNAGGTCCAGCTGCAGCAGTCTGGGGCTGAGCTTGTGAAGCTTGGGGCTTCAGTGAAGCTGTCTCTGCAAGGCT								
AAGATAAGAGTGTACGTGTCAGGTCGACGACCCGACTCGAACACTTCGGACCCCGAAGTCACCTTCGACAGGACGTTCGGA								
PheTyrSerHisSerAlaGlnValGlnLeuGlnSerGlyAlaGluLeuValLysProGlyAlaSerValLysLeuSerCysLysAla								
100	110	120	130	140	150	160	170	180
TCTGGCTACACCTTCACCAGCTACTGGATGCACCTGGGTGAAGCAGAGGCCTGGACGAGGCCTTGAGTGGATTGGAAGGATTGATCCTAAT								
AGACCGATGTGGAAAGTGGTCGATGACCTACGTGACCCACTTCGTCTCCGGACCTGCTCCGGAACCTCACCTAACCTTCCTAAGGATTA								
SerGlyTyrThrPheThrSerTyrTrpMetHisTrpValLysGlnArgProGlyArgGlyLeuGluTrpIleGlyArgIleAspProAsn								
190	200	210	220	230	240	250	260	270
AGTGGTGGTACTAAGTACAAATGAGAAGTTCAAGAGCAAGGCCACACTGACTGTAGACAAACCCCTCCAGCACAGCCCTACATGCAGCTCAGC								
TCACCAACCATGATTGTTACTCTTCAAGTTCTCGTTCGGGTGACTGACATCTGTTTGGGAGGTCGTGTCGGATGTACGTTCGAGTCG								
SerGlyGlyThrLysTyrAsnGluLysPheLysSerLysAlaThrLeuThrValAspLysProSerSerThrAlaTyrMetGlnLeuSer								
280	290	300	310	320	330	340	350	360
AGCCTGACATCTGAGGACTCTGCGGTCTATTATTGTGAAGNACGACTACGGTAGTAGCTACTACTTTGACTACTGGGGCCAAAGGGACC								
TCGGACTGTAGACTCCTGAGACGCCAGATAATAACACGTTCTATGCTGATGCCATCATCGATGATGAACACTGATGACCCCGGTTCCTCGG								
SerLeuThrSerGluAspSerAlaValTyrTyrCysAlaArgTyrAspTyrGlySerSerTyrTyrPheAspTyrTrpGlyGlnGlyThr								
370	380	390	400	410	420	430	440	450
ACGGTCACCGTCTCCCTCNGGTGGAGGCGGTTTCAGGCGGAGGTGGCTCTGGCGGTGGCGGATCCAGGCTGTTGGGACACAGGAATCTGCA								
TGCCAGTGGCAGAGGATCCACCTCCGCCAAGTCCGCCCTCCACCGAGACCGCCCTAGGTCGACAAACCCCTGTCTCTTAGACGT								
ThrValThrValSerSerGlyGlyGlySerGlyGlyGlySerGlyGlySerGlnAlaValGlyThrGlnGluSerAla								
460	470	480	490	500	510	520	530	540
CTCACCAACATCACCTGGTGAACAGTCACACTCACTTGTGCGCTCAAGTACTGGGGCTGTTTACAACACTAGTAACATATGCCAACTGGGTCCAA								
GAGTGGTGTAGTGACCACTTTGTGTCAGTGTGAGTGAACAGCGAGTTTCATGACCCCGACAAATGTTGATCATTTGATACGGTTGACCCAGGTT								
LeuThrThrSerProGlyGluThrValThrLeuThrCysArgSerSerThrGlyAlaValThrThrSerAsnTyrAlaAsnTrpValGln								
550	560	570	580	590	600	610	620	630
GAAAACCAAGATCATTTATTCACTGGTCTAATAGGTGGTACCAACACAGAGCTCCAGGTGTTCTCTGCCAGATTCTCAGGCTCCCTGATT								
CTTTTGGTCTAGTAAATAAGTGACCAGATTATCCACCATGGTTGTTGGCTCGAGGTCCACAAAGGACGGTCTAAGAGTCCGAGGGACTAA								
GluLysProAspHisLeuPheThrGlyLeuIleGlyGlyThrAsnAsnArgAlaProGlyValProAlaArgPheSerGlySerLeuIle								

640 650 660 670 680 690 700 710 720
GGAGACAAGGCTGCCCTCACCATCACAGGGGCACAGACTGAGGATGAGGCAATATATTCTGTGCTCTATGGTACAGCAACCATTTGGGTG
CCTCTGTTCCGACGGAGTGTGTCCCGGTCTGACTCCTACTCCGTTATATAAGACACGAGATACCATTGCTCGTTGGTAACCCAC
GlyAspLysAlaAlaLeuThrIleThrGlyAlaGlnThrGluAspGluAlaIleTyrPheCysAlaLeuTrpTyrnberAsnHisTrpVal
730 740 750 760 770
TTCGGTGGAGGAACCAAACTGACTGTCTCTCGAGATCAAACGGGGCGCCGC
AAGCCACCTCCTTGGTTTGACTGACAGGAGCTCTAGTTTGCCCGCCGGCG
pheGlyGlyGlyThrLysLeuThrValLeuGluIleLysArgAlaAla

Fig.45.

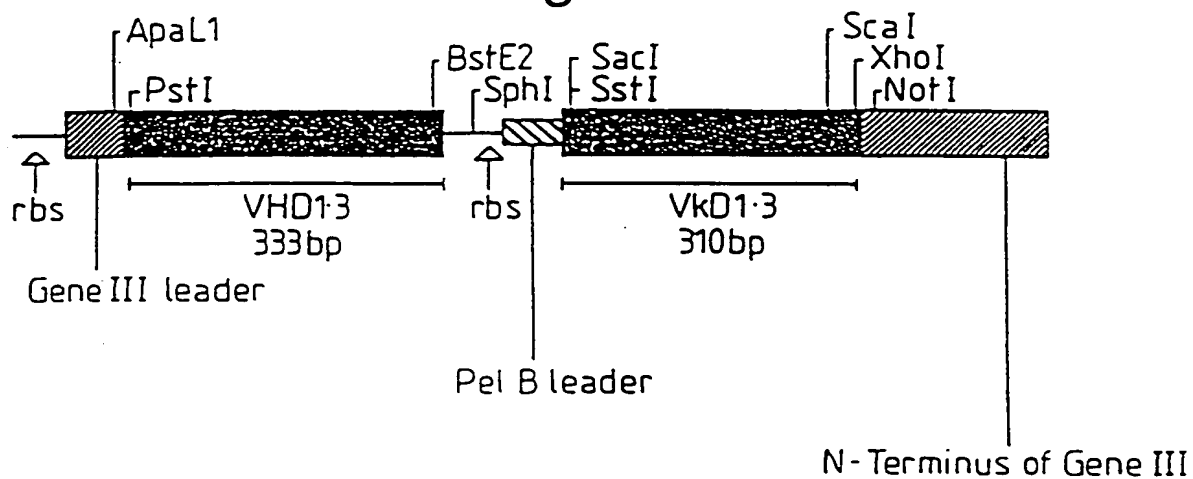


Fig.46.

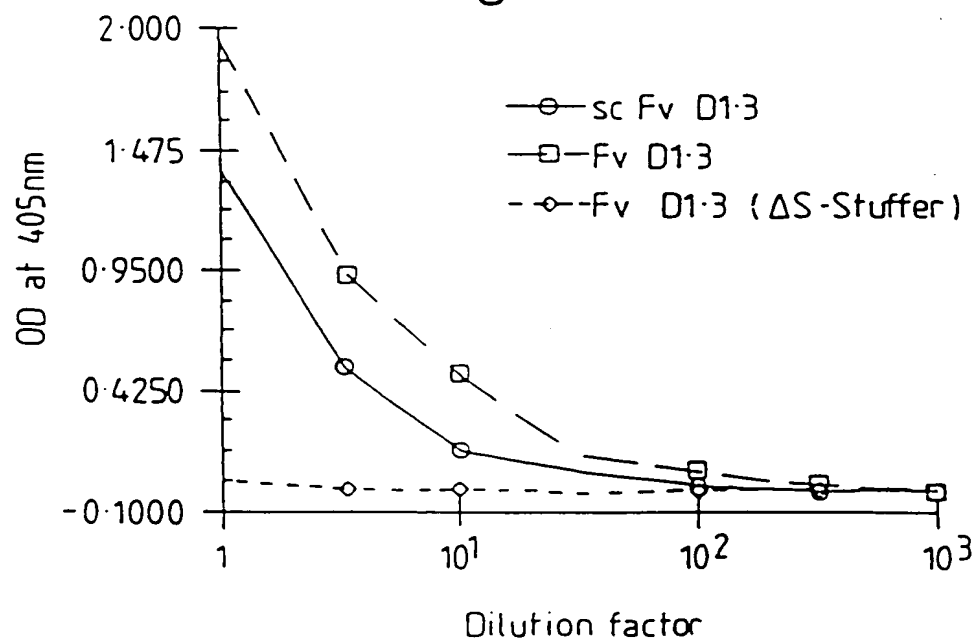
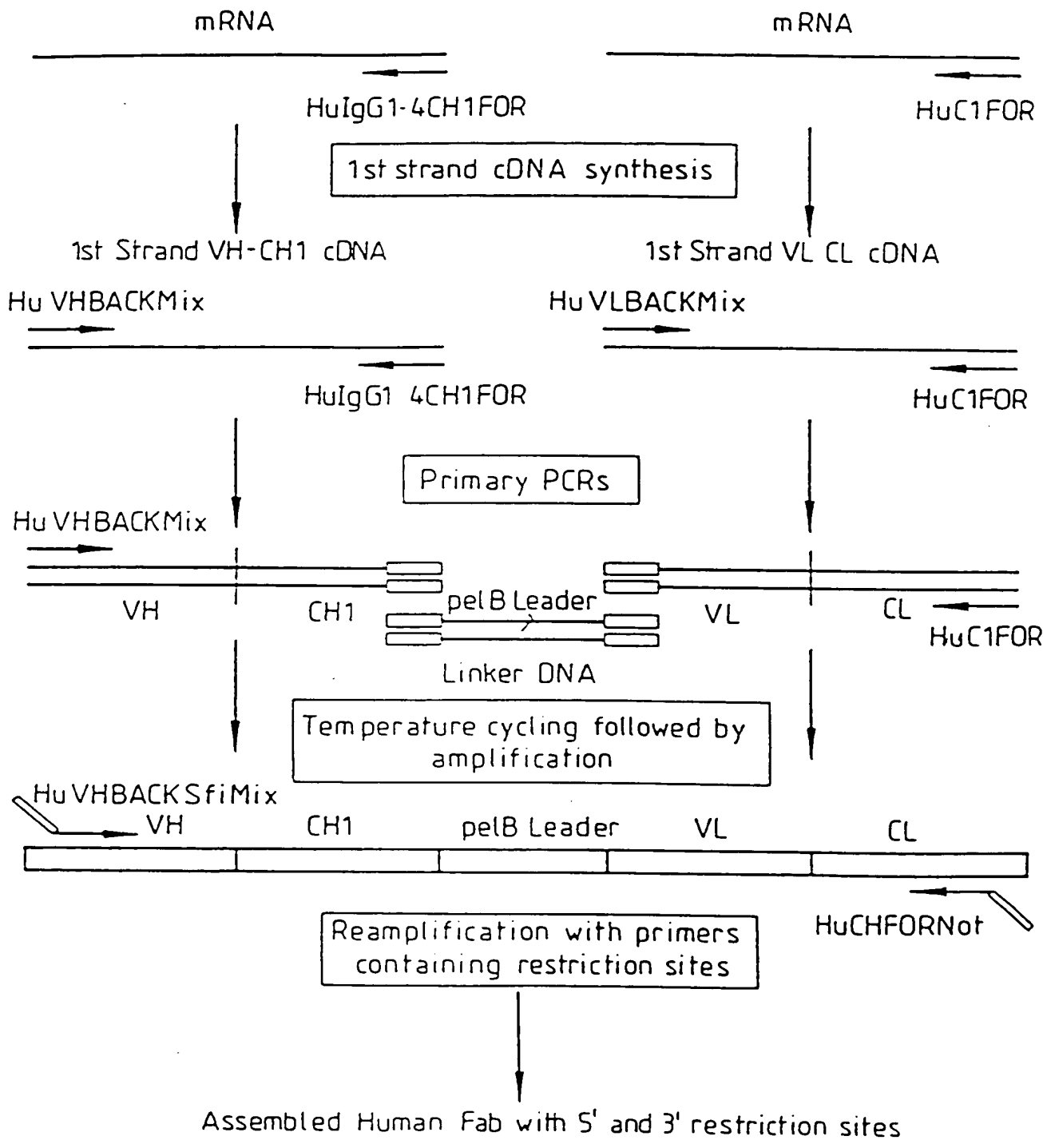


Fig.47.



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Fig.48(i)

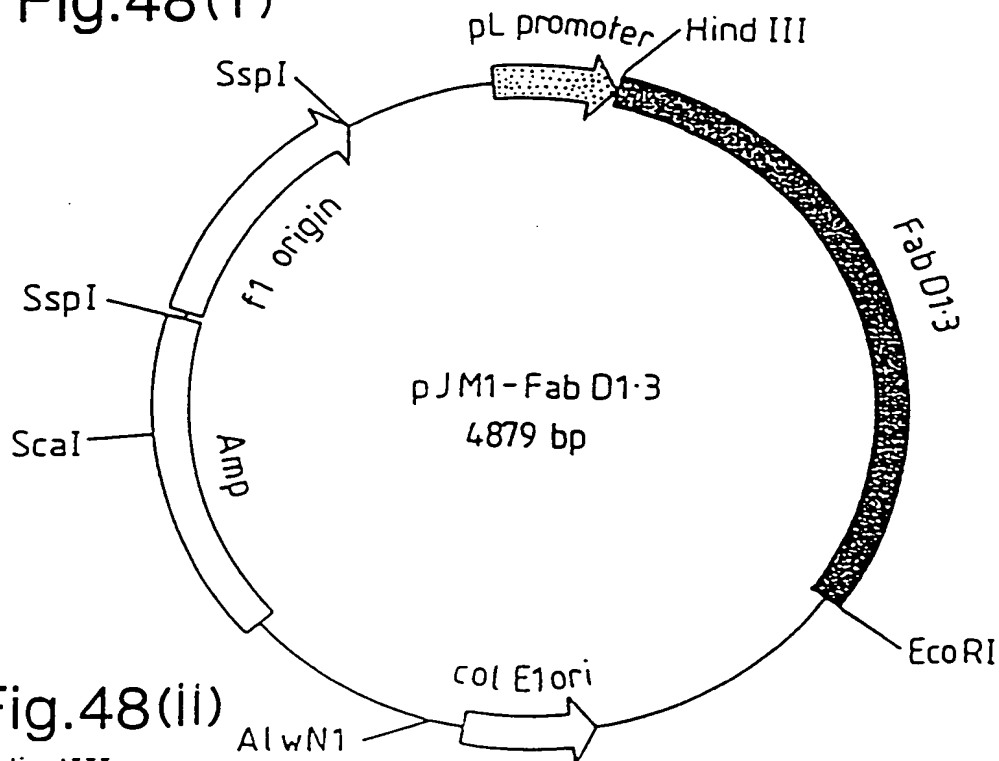


Fig.48(ii)

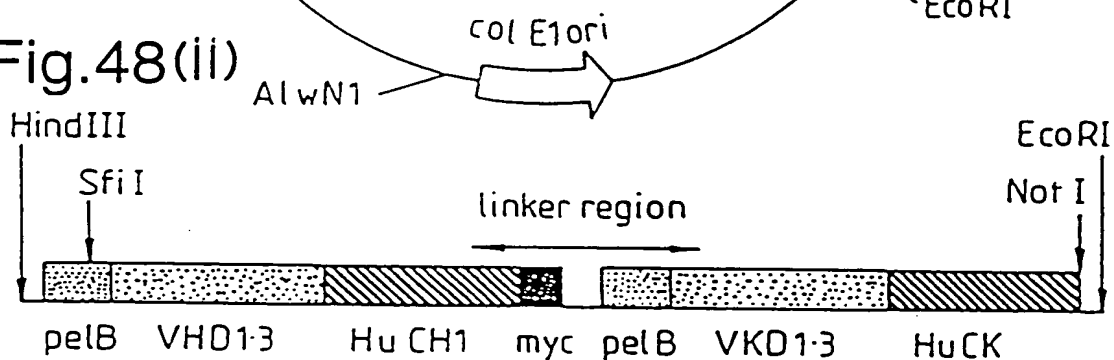


Fig.48(iii)

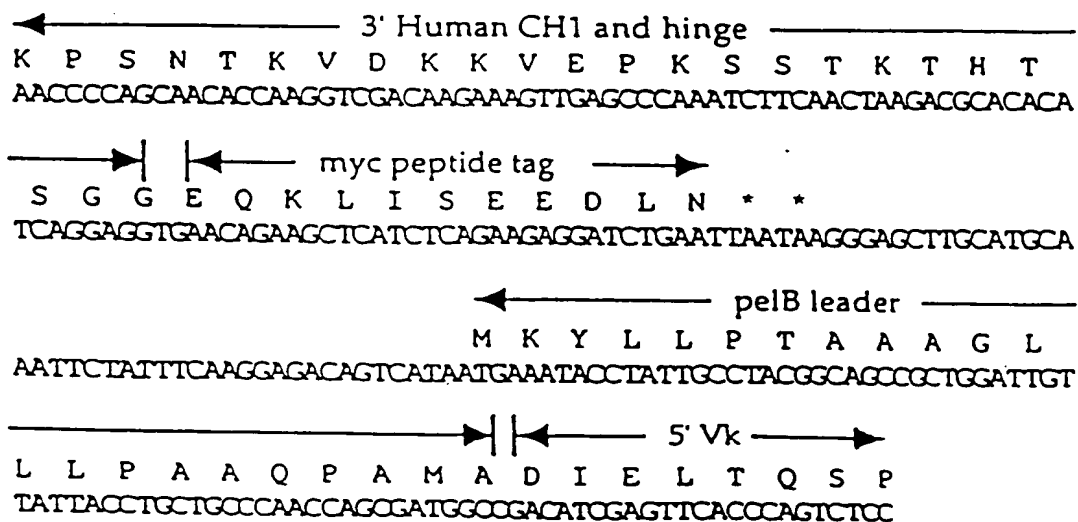


Fig.49.

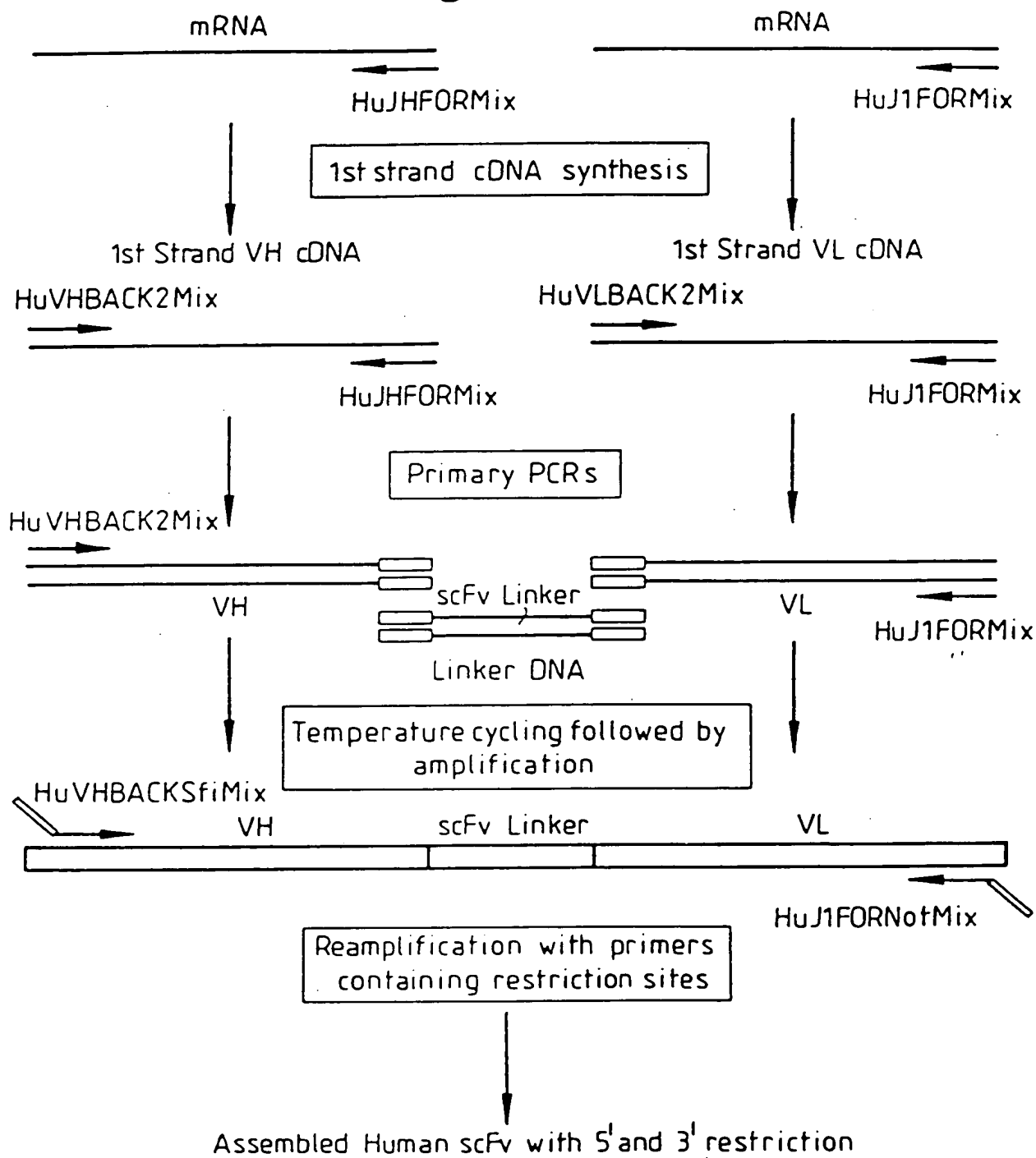


Fig.50(i)

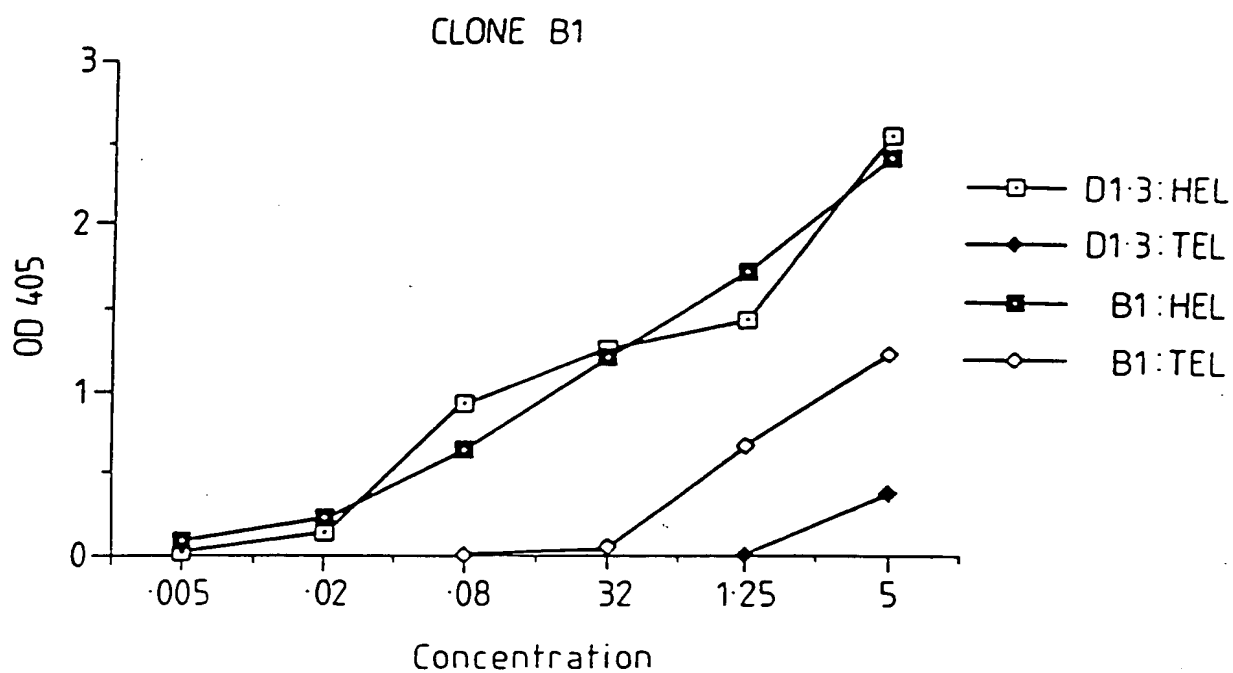
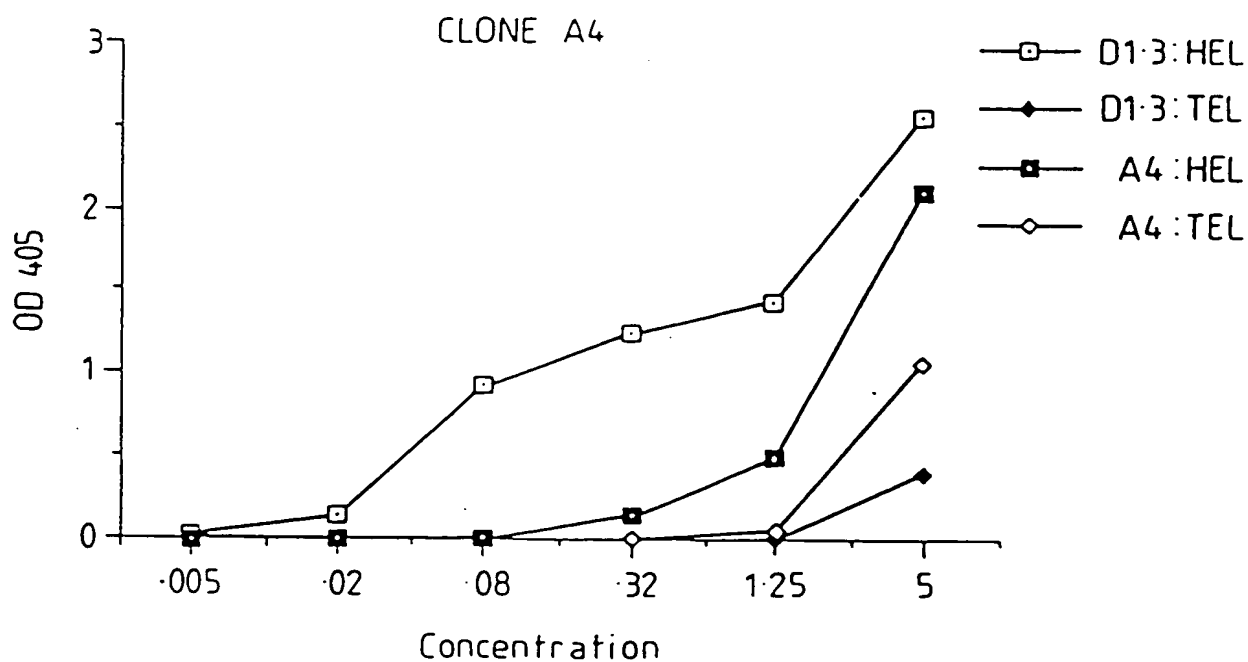


Fig.50(ii)



656707 842460

Fig.51.

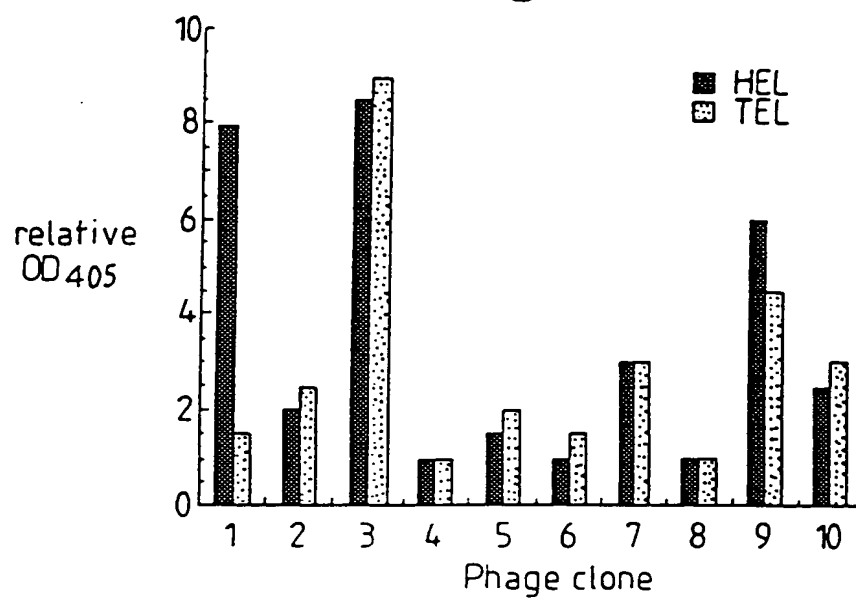


Fig.53.

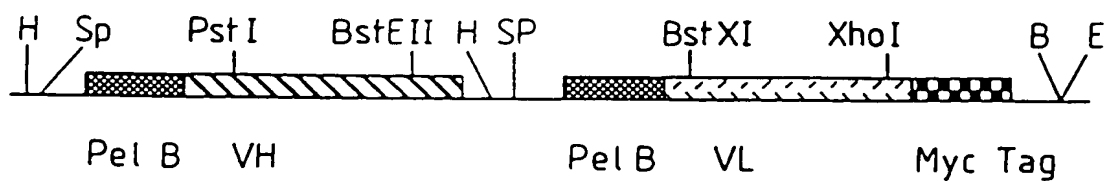


Fig.52.

	CDR 1	CDR 2
D1.3	DIQMTQSPASLSASVGETVTITCRASGNIHNYLA WYQQKQKSPQLLVYYTTTLAD	
M1F	DIELTQSPSSLSASLGERVSLTCRASQDIGSSLN WLQQEPDGTIKRLIYATSSLDS	
M21	DIELTQSPALMAASPGEKVTITCSVSSSISSNLHWYQQKSETSPKPWIYGTSNLAS	
	CDR 3	
D1.3	GVPSRFGSGGTQYSLKINSLQPEDFGSYCQHFWSTPRTFGGGTKLEIKR	
M1F	GVPKRFGSRSGSDYSLTISSESEDFVDYCYCLQYASSPWTFGGGTKLELKR	
M21	GVVPRFGSGGTSYSLTISSEAEADAATYYCQQWSSYPPLTFGAGTKLEIKR	